THE ACID-BASE METABOLISM
A NEW APPROACH

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IN this paper we evaluate factors which characterise disturbances of the acid-base metabolism. The importance of using chemical values, which are relevant from a clinical as well as a chemical point of view, is stressed and exemplified; and an analytical method is described for measuring the relevant chemical concentrations, using capillary blood, and available as a bedside procedure.

Classification of Disturbances

The term *acidosis* should denote a pathological condition due to accumulation of acid or to loss of base. These two possibilities may lead to the same clinical picture, as both tend to lower pH in the organism. Similarly, alkalosis, or better *baseosis*, should mean a pathological condition due to accumulation of base or loss of acid.

The terms " acid " and " base " are in this paper used for hydrogen-ion donor and acceptor, respectively, according to Brønsted (1923).

The use of these widely accepted definitions increases clarity (Devor 1953, Prætorius 1954, Relman 1954), especially because the acid-base metabolism can be dealt with independently of the cation metabolism. Cations are neither acids nor bases and should consequently not be designated bases (e.g., " total bases "), but cations.

Of all acids and bases, carbonic acid is physiologically unique because of its high endogenous production, and because its concentration is regulated by respiration. Disturbances primarily due to carbonic acid should therefore be clinically grouped separately. Accordingly, each of the two conditions—acidosis and baseosis—can be further classified as either *respiratory* or *non-respiratory*. The last group, often named " metabolic ", comprises all disturbances primarily due to fixed (non-volatile) acids and bases.

Primary disturbance of the acid-base metabolism is usually compensated to some extent. A respiratory disturbance is compensated by a renal mechanism, and a non-respiratory disturbance by a respiratory mechanism. If, for instance, pH tends to fall because of an accumulation of some non-volatile acid, hyperventilation lowers the arterial pCO_2 (e.g., Kussmaul's respiration). The actual state of a pathological condition can therefore be characterised also by its degree of compensation: as *not compensated* (compensatory mechanism not working), *partially compensated* (pH not brought to normal value), *fully compensated* (pH normal), or *overcompensated*.

The terms *acidæmia* and *alkalæmia* are used in some countries for conditions in which the pH of arterial blood is decreased or increased. These terms do not interfere with the classification given here.

Estimations for Diagnosis

To indicate the severity of an acid-base disorder the following estimations have proved valuable in our experience.

Arterial blood pH depends on the relation between the respiratory and the non-respiratory components of the acid-base metabolism. It thus reflects the combined influence of respiratory and non-respiratory disturbances.

Any *deviation from the normal carbon-dioxide tension* (arterial pCO_2) reflects a *respiratory* acid-base disturbance, either primary or compensatory. This accords with the general view.

Any *deviation from the normal content of base* in blood reflects a *non-respiratory* acid-base disturbance, either primary or compensatory. The base content should be expressed as *standard bicarbonate*, or as *base excess* or *base deficit*. Standard bicarbonate is the concentration of bicarbonate in plasma, when whole blood has been equilibrated with carbon dioxide at a pCO_2 of 40 mm. Hg at 38°C, and when the hæmoglobin is fully oxygenated (Jørgensen and Astrup 1957). Base excess (or base deficit) directly expresses the amount (in mEq.) of strong base (or acid) added per litre blood, when the normal mean is arbitrarily fixed at zero. Zero thus corresponds to the normal mean for standard bicarbonate (22·9 mEq. per litre). When the term base excess (B.E.) is used exclusively the *positive* values will express the excess of base, while the negative values will express the deficit of base (= excess of acid); and this makes for simplicity in practice.

The normal 95% ranges of these values are: arterial pH 7·35–7·42, arterial pCO_2 34–45 mm. Hg; standard bicarbonate 21·3–24·8 mEq. per litre; base excess −2·3 to +2·3 mEq. per litre (Siggaard Andersen et al. 1960).

When actual values found are considered the possible diagnoses are limited, and, together with clinical information, they usually lead readily to the exact diagnosis.

Standard Bicarbonate and Base Excess

The word " standard " in standard bicarbonate should signify that the bicarbonate is measured under standard conditions in order to express only the non-respiratory side of the acid-base metabolism. The standard conditions are a fixed pCO_2 and a fixed oxygenation of hæmoglobin, so that the influence of respiration on the base content of the blood is eliminated. We have chosen to measure with the hæmoglobin completely oxygenated and at a pCO_2 of 40 mm. Hg and at 38°C. If, with these conditions fulfilled, the pH of blood is measured, the Henderson-Hasselbalch equation

$$pH = 6{\cdot}10 + \log \frac{HCO_3^-}{pCO_2 \times 0{\cdot}030}$$

will give the standard bicarbonate directly when the value of pH found and the value of pCO_2 (40 mm.) chosen are inserted. Full oxygenation of hæmoglobin is chosen for convenience, and also because it eliminates the small effect of accidental variations in oxygen saturation when venous samples are drawn. The determination of standard bicarbonate is very easy (Jørgensen and Astrup 1957).

Two other bicarbonate quantities, commonly used to indicate non-respiratory disturbances, are briefly mentioned for comparison. *Total CO_2 of plasma* is the value determined by the manometric, volumetric, or titremetric techniques using plasma separated anaerobically from the cells. The value varies,

TABLE I—PLASMA VALUES FOR TOTAL CO_2, CO_2-COMBINING POWER, AND STANDARD BICARBONATE, DETERMINED IN SAMPLES FROM THE SAME NORMAL BLOOD POOL, AT PCO_2 OF 20 AND 80 MM. HG, WITH THE HÆMOGLOBIN COMPLETELY OXYGENATED AND COMPLETELY REDUCED

—	Hæmoglobin: oxygenated		Hæmoglobin: reduced	
	pCO_2 20 mm. Hg	pCO_2 80 mm. Hg	pCO_2 20 mm. Hg	pCO_2 80 mm. Hg
Total CO_2 (mM) ..	16·8	30·0	19·6	34·8
CO_2-combining power	19·0	26·7	22·0	31·4
Standard bicarbonate	21·2	21·2	21·2	21·2

Only the standard bicarbonate is independent of pCO_2 and oxygen saturation, thus showing its superiority in identifying non-respiratory disturbances.

however, with the actual pCO_2 as well as with the oxygen saturation of the blood, and can therefore not be the ideal measure of non-respiratory disturbances. This is illustrated in table I.

CO_2-combining power of plasma is the total CO_2 of plasma, which is separated from the cells at the actual pCO_2 and then equilibrated at a pCO_2 of 40 mm. Hg before measurement. This value also varies with the actual pCO_2 and the oxygen saturation, though less than total CO_2 (table I).

Thus it seems evident that standard bicarbonate is the best *bicarbonate* value to measure when it is desired to eliminate the influence of the respiration and to determine the non-respiratory component only. The effect of equilibrating whole blood seems to be approximately the same in vitro as in vivo (Shock and Hastings 1935)—i.e., as if the respiratory function was standardised.

The standard bicarbonate value has, like other bicarbonate values, the drawback that it does not show directly the amount, in mEq. per litre blood, of fixed acid or base causing a change in the base content of a blood sample. (This is because the carbon-dioxide/bicarbonate system is responsible for only about 75% of the buffer action of the blood against fixed acids and bases, when the pCO_2 is kept constant (see table II)). Therefore, to find the total deficit or excess for base per litre blood, the deviation of standard bicarbonate from the normal mean must be corrected; this can be approximately achieved by multiplying by 1·20. An exact correction requires knowledge of the buffer capacity of the blood—i.e., the hæmoglobin concentration. The advantage of using quantities which directly give the surplus amount of fixed acids or bases contained per litre blood is thus evident. Here the use of change in buffer base or of base excess is helpful.

Buffer base (Singer and Hastings 1942), which in all cases should be used in the form agreeing with the acid-base concept of Brønsted (1923), includes buffer anions other than bicarbonate, especially hæmoglobinate ions. Thereby its value becomes independent of pCO_2, and a *change* in buffer base, in mEq. per litre, directly expressed the amount of acid or base causing the change (table II). On the other hand, it represents a sum of factors of different buffer capacities. Furthermore, *the buffer base value of a blood sample depends on its hæmoglobin and protein concentration* (table II). A patient with a low buffer-base value due to a low hæmoglobin concentration thus needs hæmoglobin and not bicarbonate.

Concerning the quantity *base excess* (for definition see above), this gives directly, in mEq. per litre blood, the surplus amount of fixed acid or base (table II). It is a quantity easily understood by those unfamiliar with clinical acid-base problems. Further it allows the treatment of acid-base problems in a quantitative way. So, from both a theoretical and a practical point of view, base excess is preferable to buffer base. One argument against the use of base excess is that it does not give an ion-value for the base-concentration in blood. If this is wanted the standard bicarbonate should be used, thus giving the bicarbonate concentration of plasma under standard conditions.

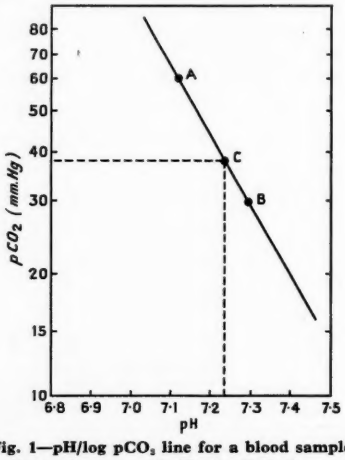

Fig. 1—pH/log pCO_2 line for a blood sample.

Point A indicates the measured pH value 7·12 after equilibration at pCO_2 = 60 mm. Hg. Similarly point B indicates pH 7·30 at pCO_2 = 30 mm. Hg. If, for instance, the actual pH of the anaerobically drawn blood had been measured to 7·24, the actual pCO_2 would be read as 38 mm. Hg (point C).

Total CO_2, CO_2-combining power, standard bicarbonate, buffer base, and base excess can be determined by the new microtechnique outlined below.

Quantitative Treatment of Acid-base Disturbances

Respiratory Disturbances

Changes in the alveolar ventilation, leading to respiratory disturbances, are determined quantitatively by the pCO_2 of arterial blood, the value of which in general can be assumed to be identical with the value of pCO_2 of alveolar air.

As the excreted amount of carbon dioxide per time unit is constant for an individual in a steady state, the

TABLE II—VALUES FOR BUFFER BASE, BASE EXCESS, AND STANDARD BICARBONATE, DETERMINED IN BLOOD SAMPLES WITH DIFFERENT CONCENTRATION OF HÆMOGLOBIN (15 AND 7·5 G. PER 100 ML.) AND WITH OR WITHOUT ADDITION OF STRONG ACID AND BASE (10 MEQ. PER LITRE BLOOD)

—	Blood with 15 g. hæmoglobin per 100 ml.			Blood with 7·5 g. hæmoglobin per 100 ml.		
	No acid or base added	10 mEq. strong acid added per litre blood	10 mEq. strong base added per litre blood	No acid or base added	10 mEq. strong acid added per litre blood	10 mEq. strong base added per litre blood
Buffer base (mEq. per litre blood)	46·2	36·2	56·2	43·4	33·4	53·4
Base excess (mEq. per litre blood)	0	−10	+10	0	−10	+10
Standard bicarbonate (mEq. per litre plasma) ..	22·9	15·9	30·7	22·4	15·4	31·0

The blood samples were obtained from a pool of normal blood (kept at 38°C, at pCO_2 = 40 mm. Hg, and with the hæmoglobin completely oxygenated) The hæmoglobin concentration was altered by adding plasma.

product of the alveolar ventilation (A) and the pCO_2 of the arterial blood has a constant value (K): $A \times pCO_2 = K$. Accordingly, if the alveolar ventilation decreases, the pCO_2 must increase, and vice versa. For instance, a decrease of A to half must double the pCO_2.

In some cases additional laboratory measurements help in elucidating the cause of a respiratory disturbance. Among these the measurement of the oxygen saturation or the oxygen tension (pO_2) of arterial blood is important. Thus, a low oxygen saturation with a low pCO_2 is associated with completely different diseases to a low oxygen saturation with a high pCO_2.

Non-respiratory Disturbances

When dealing with the *non-respiratory disturbances*, knowledge of the total amount of excess acid or base in the organism can be of clinical importance. The problems involved are rather complex, and for proper treatment knowledge of the distribution of acid and base in the different body-spaces and the rate of exchange between them is required. The following approximations are helpful.

The deficit or excess of base in *the extracellular body-space* can be estimated in mEq. by multiplying the negative

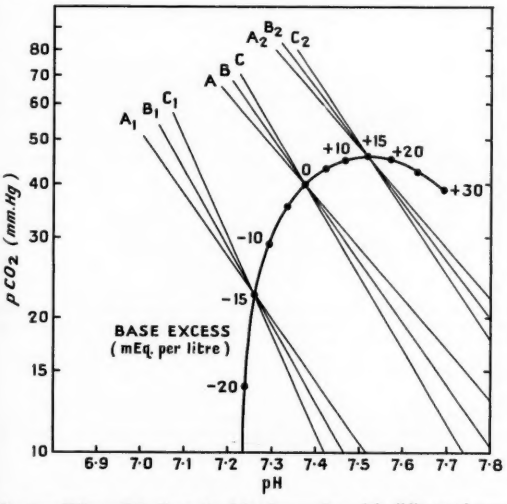

Fig. 2—pH/log pCO_2 lines for blood samples with different hæmoglobin concentration and different content of base.

A, B, and C represent samples of normal blood with a hæmoglobin concentration of 0, 10, and 20 g. per 100 ml. respectively. A_1, B_1, and C_1 show the displacement after addition of fixed acid (15 mEq. acetic acid per litre blood); and A_2, B_2, and C_2 after addition of base (15 mEq. sodium carbonate per litre blood). The points of intersection of these lines form a curve (the base-excess curve) which indicates the amount of base excess (positive values) and base deficit (negative values) in any blood sample.

or positive value found for base excess, in mEq. per litre blood, by 0·3 × the body-weight in kg., where the factor 0·3 is found experimentally (Mellemgaard and Astrup 1960). This amount corresponds directly to the amount of sodium bicarbonate or of ammonium chloride required to neutralise a non-respiratory disturbance in the *extracellular space*.

For *the whole body*, the factor 0·7 should be used instead of 0·3 (Palmer and Van Slyke 1917).

In dealing with patients, however, the amount of excess or deficit of base in the whole body does not always seem to be directly proportional to the excess or deficit of base in the

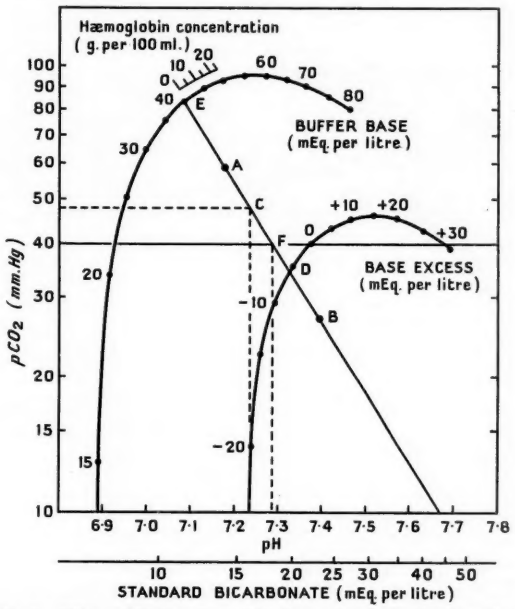

Fig. 3—pH/log pCO_2 line for a blood sample, determined as described in fig. 1.

The point of intersection (D) with the base-excess curve indicates the amount of base excess to be −6·0 mEq. per litre blood, while point E indicates the buffer base (= 40 mEq. per litre). The standard bicarbonate (18·6 mEq. per litre) can be derived from the pH value corresponding to pCO_2 = 40 mm. Hg (F). The abscissa shows pH values and standard bicarbonate. The total CO_2 of the plasma from the anaerobically drawn blood and the CO_2-combining power can be found from the figure. (For this calculation see Siggaard Andersen and Engel 1960.)

blood. When, therefore, patients are to be treated with intravenous infusions of acid or base, it is advisable to estimate the dose necessary to normalise the base content of the extracellular space only, and then follow the effect of the treatment by frequent blood analyses and also by clinical observation, before new infusions are given. Thus overtreatment is avoided (Mellemgaard and Astrup 1960).

In treating the non-respiratory disturbances, it is important to estimate an abnormal loss of acid or base. This is especially so when the loss is extrarenal—e.g., in

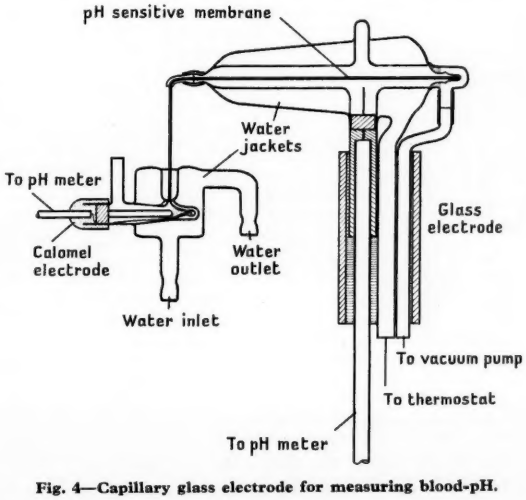

Fig. 4—Capillary glass electrode for measuring blood-pH.

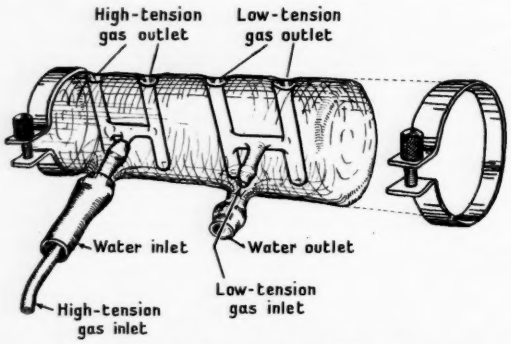

Fig. 5—Chamber for simultaneous equilibration of microsamples in duplicate at two different carbon-dioxide tensions.

pyloric stenosis and pancreatic fistula. In such cases the lost amount of acid or base should be determined by titration together with the twenty-four-hour excretion of acid or base in urine (Jørgensen 1957).

Micromethod for Determining pH, pCO_2, Standard Bicarbonate, and Base Excess

When using macromethods for determining the above relevant values for characterising the acid-base status, arterial punctures are necessary. This is a drawback when frequent analyses are needed—for instance at intervals of minutes in cases with rapid changes in the respiration (in anæsthesiology, treatment in a respirator, &c.). A micromethod, using about 100 µl. blood, was therefore developed (Siggaard Andersen et al. 1960).

Principle

The theoretical background for the calculation of pCO_2, standard bicarbonate, and base excess is that graphs showing the relations between log pCO_2 and pH are approximately straight lines (shown experimentally by Brewin et al. 1955 and Astrup 1956). The slope of the lines depends on the buffer capacity of the blood. By equilibrating a blood sample at two known CO_2 tensions and measuring the pH values, the line for the sample is determined (fig. 1). If the actual pH of the blood sample is known, then the actual pCO_2 can easily be found.

When fixed acid is added to the blood, the line is displaced to the left. When base is added, the line is displaced to the right. Now a graph (fig. 2) can be constructed expressing the displacement caused by any amount of acid or base, independent of the hæmoglobin concentration (Siggaard Andersen and Engel 1960).

The point of intersection between this curve and a found pH/log pCO_2 line for a blood sample thus indicates, in mEq., the base excess per litre blood.

In the same diagram a curve can be constructed (Siggaard Andersen and Engel 1960) expressing the content of buffer base according to the definition of Singer and Hastings (1948). The curve is shown in the upper left corner in fig. 3. By using this curve the amount of buffer base in blood can be found.

Thus exact measurement of blood pH at the actual pCO_2 and at two known values for pCO_2 will allow the calculation of *all* relevant blood data concerning the acid-base status. This is illustrated in fig. 3.

Equipment for Determination at Bedside

The equipment is described in detail elsewhere (Siggaard Andersen, et al. 1960). It consists of a pH-meter, a circulating thermostat, a suction pump, a micro-electrode (fig. 4) according to Sanz (1957), and a micro-equilibration chamber (fig. 5). All these parts can be mounted on a portable table together with two small cylinders containing mixtures of oxygen and carbon dioxide.

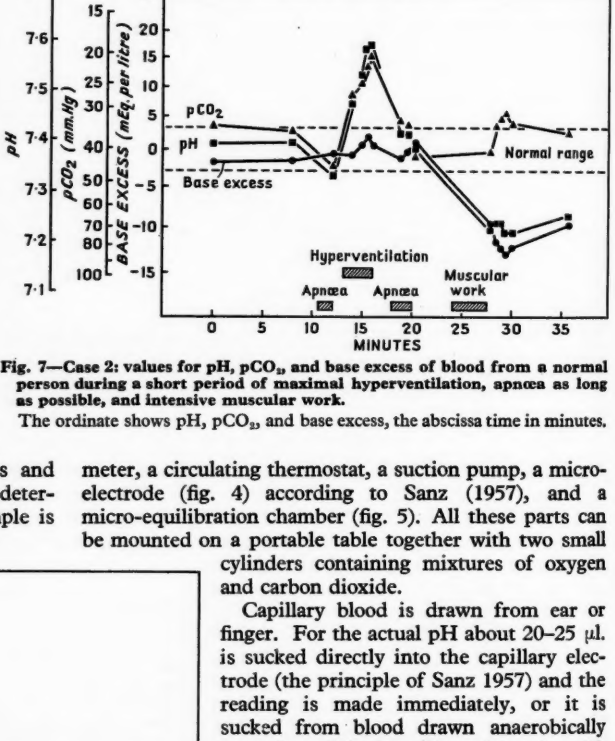

Fig. 7—Case 2: values for pH, pCO_2, and base excess of blood from a normal person during a short period of maximal hyperventilation, apnœa as long as possible, and intensive muscular work.

The ordinate shows pH, pCO_2, and base excess, the abscissa time in minutes.

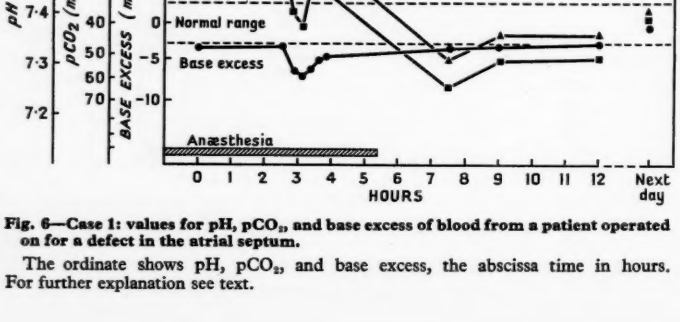

Fig. 6—Case 1: values for pH, pCO_2, and base excess of blood from a patient operated on for a defect in the atrial septum.

The ordinate shows pH, pCO_2, and base excess, the abscissa time in hours. For further explanation see text.

Capillary blood is drawn from ear or finger. For the actual pH about 20–25 µl. is sucked directly into the capillary electrode (the principle of Sanz 1957) and the reading is made immediately, or it is sucked from blood drawn anaerobically into a heparinised capillary glass tube with sodium fluoride. About 80–90 µl. of blood from two capillary glass tubes is divided between two of the chambers in the equilibration apparatus. This is then shaken mechanically (2600 r.p.m.) and after three minutes the pH values in the two samples are measured successively. By using these two values and the corresponding pCO_2 values (from the cylinders), the pH/log pCO_2 line is drawn and the pCO_2, standard bicarbonate, and base excess can be calculated (fig. 3). The method is

highly accurate, as the three values can be found with an error of less than ±2%.

Illustrative Cases

The advantage of frequent registration of pH, pCO_2, and base excess by the method described here is illustrated in the following two cases. Figs. 6 and 7 show a convenient graphic system for these three quantities.

Case 1.—Fig. 6 shows blood values from a patient (female, 15 years old) operated on for a defect in the atrial septum. At the beginning of the operation the values for the non-respiratory component indicate a slight base deficit, possibly due to the postabsorptive phase. A manifest non-respiratory acidosis develops as soon as the blood of the patient is mixed with the rather acid donor blood from the heart-lung machine (approximately 4 litres with a base excess of −12 mEq. per litre, mainly due to lactic acid). The acid excess quickly decreases, partly by distribution between the different body compartments, and partly by oxidation of the lactic acid. The second day after the operation a normal value is reached.

The curve for the respiratory component (pCO_2) shows first the effect of overventilation during the anæsthesia. A slight rise in pCO_2 is seen when the heart-lung machine is responsible for the CO_2 excretion. When spontaneous respiration was established after the operation the pCO_2 was between 50 and 60 mm. Hg, reaching a normal value within a few hours.

The pH curve shows the resulting action of the respiratory and non-respiratory components on the hydrogen-ion concentration.

Case 2.—The pronounced deviations from normal acid-base values seen in a normal individual (male 26 years old) by maximal hyperventilation, periods of apnœa, and intensive muscular exercise of short duration are illustrated in fig. 7.

The rise in pCO_2 and the fall in pH during the two apnœa periods are moderate and obviously the fall in oxygen saturation (to about 80%, not measured accurately) is the limiting factor for the length of voluntary suspension of breath. During hyperventilation a fall in pCO_2 to about 20 mm. Hg was observed. The muscular exercise was followed by enormous hyperventilation, but the pCO_2 was now practically within normal limits. The explanation must be that the greatly increased CO_2 production is compensated by an equally increased CO_2 excretion by means of the hyperventilation.

Only small variations, within the normal limits, are seen during the pure respiratory changes. A possible cause of these small variations is displacement of base between the different body-spaces; this point deserves further investigation. During the muscular exercise a heavy non-respiratory acidosis develops, with a base excess of −12 mEq. per litre, indicating accumulation of large amounts of lactic acid.

Great fluctuation in the pH from 7·58 and 7·21, observed over a period of ten to fifteen minutes, was caused exclusively by a fall in pCO_2 and in base excess.

Summary

Disturbances in the acid-base metabolism have been classified according to the relation between blood values for pH, pCO_2, and an index of non-respiratory disturbances. This index should be either bicarbonate concentration measured under standard conditions as "standard bicarbonate" or else the surplus amount, as "base excess", of fixed acid or base in mEq. per litre blood. Knowledge of the value of base excess enables the total deficit or excess of base in the blood-volume and in the extracellular space to be calculated.

An accurate bedside method, using capillary blood, for determining all relevant blood values for the identification of disturbances in the acid-base metabolism, qualitatively and quantitatively, has been devised.

References at foot of next column

MEDICAL ASPECTS OF ROAD SAFETY *

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To drive safely requires the use of certain physical and mental qualities in reasonable degree. But these qualities can seldom be precisely defined and they cannot be quantified. Perhaps the nature and amount of the eyesight required for driving have been more fully established than those of other qualities, but even here the borderline between fitness and unfitness to drive is somewhat arbitrary.

In Great Britain in 1958 the police reported 992 road accidents in which a driver was ill or in which his physical defect was regarded as a contributory cause (Road Accidents 1958). This is a small proportion of the total number of accidents, but their prevention is of particular medical interest.

The clinical assessment of fitness to drive does not involve the development of yet another branch of Medicine. It is simply the application of clinical knowledge to the particular requirement of driving vehicles safely; and, as almost all doctors drive themselves, they are in the fortunate—and unusual—position of having practical experience of both sides of this question. Many adult patients are drivers who may seek advice on their fitness to drive during convalescence or in relation to chronic disease. This is especially important for professional drivers who may be responsible for the safety of many passengers.

A general guide for physicians on the assessment of fitness to drive has been published by the American Medical Association (1959) which has also produced a bright little booklet for patients, entitled "Are You Fit to Drive?". The British Medical Association (1954) and the World Health Organisation (1956) have also published helpful guides for physicians. These are not as well known as they should be.

In assessing the fitness of drivers it is usual to consider three types of vehicle: (1) the public-service vehicle in which seventy or more passengers may be carried, (2) the heavy commercial vehicle, and (3) the private car. The driver of public-service and commercial vehicles is a professional who generally drives for several hours a day; the private-car driver is usually an amateur whose driving may be for as little as half an hour a week or as much as eight hours a day—for example, some sales representatives. The risk of accident due to a medical condition in a driver increases with the time he spends driving. Hence, in assessing the fitness of patients to

* The second Milroy lecture for 1960, delivered before the Royal College of Physicians of London on Feb. 4. The first lecture appeared last week.

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TABLE VI—LONDON TRANSPORT DRIVERS: MEDICAL EXAMINATIONS AT CERTAIN AGES, 1959

—	Age											
	50		56		62		64		65–69		All ages	
	Examined	Found unfit	Examined	Found unfit	Examined	Found unfit	Examined	Found unfit	Examined	Found unfit	Examined	Found unfit
No. of drivers	606	7 (1·1%)	515	15 (2·9%)	315	20 (6·3%)	195	9 (4·6%)	499	22 (4·4%)	2130	73 (3·4%)

drive, it is reasonable to take into account the number of hours a week for which they drive. Higher standards of fitness are necessary for drivers of public-service vehicles, who have to obtain a medical certificate of fitness before their licence is issued (P.S.V. Regulations 1934). Their medical examinations were described by Raffle (1959).

Road-service drivers in London Transport are medically examined at the ages of 50, 56, 62, 64, and annually thereafter (Norman 1958). The results in 2130 drivers examined in 1959 are shown in table VI. Of the 73 who were found unfit, cardiovascular conditions were responsible in 51, visual defects in 7, arthritis in 2, diabetes in 2, and a variety of conditions in the remaining 11. Such drivers were recommended for other work. As might be expected, a much higher proportion—23·6%—of drivers returning to work after illness were found unfit, temporarily or permanently. Drivers need adequate convalescence after illness, both for their own safety and for that of other road users. Sometimes their convalescence is too short because they want to return to full earning capacity.

Loss of Consciousness While Driving

Assessment of fitness to drive is directed particularly at detecting conditions which may cause a sudden loss of consciousness. These include:

Simple faint (syncopal attack).
Cerebral anoxia (perhaps anæmia).
Falling asleep (and narcolepsy).
Postural hypotension:
  (*a*) Ganglion-blocking agents.
  (*b*) Splanchnic pooling.
Psychogenic episode (hysteria).
Hæmorrhage into cerebral tumour.
Aortic stenosis or regurgitation.
Pulmonary embolism.
Carotid-sinus syncope.
Poisoning (e.g., carbon monoxide).
Laryngeal vertigo (cough syncope).
Intestinal hæmorrhage:
  (*a*) Massive.
  (*b*) Slight recurrent, leading to syncope.
Head injury: (*a*) Subdural hæmatoma.
Cerebrovascular accidents.
Subarachnoid hæmorrhage.
Epilepsy:
  (*a*) Idiopathic.
  (*b*) Space-filling lesion—e.g., secondary to bronchial carcinoma.
  (*c*) Triggered off by hypoglycæmia, alkalosis, or hypocalcæmia.
Abnormal cardiac rhythm:
  (*a*) Stokes-Adams attacks.
  (*b*) Rarely auricular flutter or paroxysmal tachycardia.
Myocardial infarction.
Dissection of the aorta.
Hypoglycæmia:
  (*a*) Insulin.
  (*b*) Spontaneous.
  (*c*) Reactive.

In the eleven years 1949–59 London Transport has employed an average of about 20,000 drivers, whose experience thus amounts to about 220,000 driver-years. In this period there were 46 cases in which a driver lost consciousness suddenly while driving. Lest this figure be thought rather high, I should point out that the average passenger would have had to ride for about an hour a day for nearly thirty-five thousand years before being involved in such an accident. A summary of these cases is given in table VII. The ages of the drivers ranged from 36 to 63, with no particular prevalence in any one age-group; only 5 were over 60. The following case illustrates the type of investigations made after an incident of this kind:

A man aged 47 was driving a bus one evening when he lost consciousness suddenly. The bus is thought to have been out of control for about 60 yards, and, swerving to the offside of the road, it demolished about 20 yards of low wall. Nobody was injured. When the driver recovered consciousness a few minutes later, he remembered nothing of the incident. He was under treatment for a duodenal ulcer, and for fear of vomiting he had not eaten any food that day. In hospital it was thought that dehydration, alkalosis, and hypoglycæmia together had triggered off an epileptic attack. Other work with no driving was found for him.

Hypertension

Little is known of the relation, if any, between accident-rates and blood-pressure. Blood-pressure measurements are therefore directed towards prediction of such events as cerebrovascular accidents, coronary infarction, dissection of the aorta, Stokes-Adams attacks, vertigo, and fainting. Any of these conditions, occuring without sufficient warning may result in a serious accident. Though such conditions are not directly related to the blood-pressure there is a level of pressure at which the risk of cerebrovascular accidents is too high to accept. The difficulty is to define this critical level, especially where blood-pressure readings are casual ones taken in the consulting-room. Moreover, emotional disturbances while driving may raise the blood-pressure.

In 1958, a man aged 58 was driving a bus when he suddenly lost consciousness and the bus collided with a trolleybus standard. There was no previous history of illness and the sickness record showed only occasional minor absences. He died without regaining consciousness and necropsy revealed a large cerebral hæmorrhage with evidence of gross hypertension. He had attended the medical department only for routine eyesight tests, and his blood-pressure had not been recorded. Under present arrangements his hypertension would have been found at routine age examinations.

TABLE VII—DIAGNOSIS IN CASES WHERE DRIVERS LOST CONSCIOUSNESS, 1949–59

Diagnosis	No. of cases	No. of cases in which collision or other accident resulted
Coronary infarction	14	3
Laryngeal vertigo	2	2
Whooping-cough	1	1
Lobar pneumonia	1	..
Hypertensive encephalopathy	1	1
Probable epilepsy	8	8
Reflex hypotension from muscular cramp	1	1
Simple faint (vasovagal syncope)	5	5
Subarachnoid hæmorrhage	1	1
Cerebral hæmorrhage	1	1
Reactive hypoglycæmia	1	1
Onset of febrile illness (" influenza ")	1	1
Convalescent after illness (" influenza ")	1	..
Unknown	8	1
Total	46	26

In two other cases in which men lost consciousness while driving, the only abnormality found was hypertension, the blood-pressures being 255/140 and 280/130 mm. Hg respectively.

The World Health Organisation (1956) recommends that in essential hypertension, where the systolic pressure is persistently above 200 mm. Hg or the diastolic pressure persistently above 100 mm. Hg, driving of a heavy motor vehicle should not be permitted. This view may be too rigid. The American Medical Association guide says that hypertension in itself does not interfere with the safe operation of a motor vehicle, but that " complications arising from hypertension, i.e., damage to brain, eyes, heart or kidneys, may well prove to be so disabling ". The A.M.A. also recommends that when " the complications of hypertension are limited to the optic fundi, the degree of impairment of driving ability should be evaluated solely on the basis of loss of vision ". However, ophthalmoscopy is essential for the assessment of the significance of hypertension.

In assessing the fitness of public-service drivers, a level of hypertension has been chosen which is regarded as borderline; ten other factors are then taken into consideration. The borderline case is that of a man aged 55, with a systolic pressure of 210 mm. Hg or a diastolic pressure of 105 mm. Hg. Below these levels he is considered fit to continue driving, but if he is near either level he is again examined in six or twelve months. The driver rests for at least fifteen minutes before readings are taken, and two measurements at a week's interval may be made. Corrections for arm circumference are not normally applied and measurements are usually made on one arm only. To avoid creating anxiety, measurements are generally not repeated more than once during any one examination.

The ten factors taken into consideration are:

1. *Age.*—As the risk of cerebrovascular accidents increases with advancing age, the borderline level becomes 200 mm. Hg systolic or 100 mm. diastolic at the age of 65.

2. A *family history* devoid of cerebrovascular and cardiovascular troubles improves the prognosis.

3. *Symptoms.*—Mild occipital headaches are not regarded as significant. A history of angina pectoris, vertigo, " stroke ", transient loss of cerebral function, or any residual neurological abnormality on examination, is a bar to driving.

4. *Fundus oculi.*—Retinopathy of grades III and IV would generally bar from driving.

5. *Albuminuria* of more than a trace worsens the prognosis and the driver is certified unfit.

6. *Glycosuria*, if present, does not adversely affect hypertension and is dealt with as given under Diabetes (see below).

7. *Overweight*, if more than 20% above the life-assurance standards (Conduct of Life Assurance Examinations 1949), is an adverse factor.

8. *Organic arrhythmias*, if present, generally bar from driving.

9. *Electrocardiogram.*—Gross abnormalities bar from driving.

10. *Chest radiograph.*—Cardiac enlargement of more than minor degrees bars from driving.

Broadly similar recommendations for public-service drivers were made by the Royal Australian College of Physicians (1959). The standards for public-service drivers are more strict than those which should probably be applied in advising private-car drivers. For the latter, hypertension, unless extreme or accompanied by complications, is not usually considered a bar to driving.

During 1959, 39 London Transport drivers were found unfit because of hypertension. Blood-pressure readings ranged from 180/120 to 260/150, and the majority also showed evidence of hypertensive vascular disease. Only 1 of these drivers was over the age of 65—presumably because most hypertensives had been eliminated at previous examinations.

Ischæmic Heart-disease

About a third of cases of loss of consciousness when driving are due to coronary infarction. In 1949–59 among some 20,000 London Transport drivers 14 cases occurred (table VIII).

That there were only 14 cases in 220,000 driver-years of exposure emphasises the small size of the risk, but in an undertaking as large as London Transport this amounts to about one case in every ten months. Of the 12 cases in which the vehicle was moving, there were 5 where the driver did not seem to have enough warning to stop the vehicle, and 3 of those resulted in accidents. Morris et al. (1952 and 1957) and Morris (1958), in their study of doctors, showed that the risk of a second coronary episode may be ten times as high as the risk of a first. Hence a diagnosis of myocardial infarction excludes a man from driving public-service vehicles. Unequivocal electrocardiographic changes indicating previous myocardial infarction also exclude him, whether he has symptoms or not. The Royal Australian College of Physicians (1959) and the American Medical Association (1959) agree with these views.

TABLE VIII—DRIVERS EXPERIENCING LOSS OF CONSCIOUSNESS DUE TO CORONARY INFARCTION WHILE DRIVING, 1949–59

Case no.	Any collision or damage?	Did driver have sufficient warning to stop the vehicle?
1	No	Vehicle stationary
2	No	No
3	No	Yes
4	No	Yes
5	Yes	No
6	Yes	No
7	No	Yes
8	No	No
9	Yes	No
10	No	Yes
11	No	Yes
12	No	Yes
13	No	Yes
14	No	Vehicle stationary

A diagnosis of angina pectoris should exclude a man from driving public-service vehicles. The risk of sudden loss of consciousness while driving is probably as great in such a person as in one who has recovered from myocardial infarction.

Electrocardiograms are not taken for London Transport drivers as a routine, but only when clinically indicated.

Apart from variation in the interpretation of electrocardiograms (Davies 1958) there is the practical difficulty that perhaps as many as 20% of men over 50 show minor abnormalities. Changes after exercise, of a degree usually held to indicate coronary heart-disease, were found by Acheson (1957) in 15% of fit symptomless R.A.F. men aged 20–40. Whether these changes are an indication of future coronary disease will not be known until these men have been observed for a further long period. To exclude all drivers with minor electrocardiographic abnormalities would be unfair in most cases and would seriously deplete the numbers of drivers available to the undertaking.

To take an electrocardiogram when a driver is first employed would probably be helpful, both to serve as a baseline for later investigation and to establish the existence of unimportant congenital variations such as left bundle-branch block.

By various examinations one can select a small proportion of the population who are symptomless but who have hypertension, a family history of coronary heart-disease, and a high blood-cholesterol (especially the β-lipoprotein fractions), and are overweight. At present it is not thought justifiable to remove such men from

driving; but if further research reveals a small proportion of drivers who carry a very high risk this problem will have to be reconsidered. What probably matters most is whether the driver is genetically equipped to deal with cholesterol, and this cannot yet be ascertained.

It is generally held that people who have made a good recovery from coronary infarction, or whose attacks of angina are mild and infrequent may continue to drive private cars.

Epilepsy

The applicant for a licence must answer the question "Do you suffer from epilepsy, or from sudden attacks of disabling giddiness or fainting?" A patient who is under treatment and has had no fits for two years might well answer "No" to this question, which could usefully be reworded, "Have you ever suffered from epilepsy . . . ?". Driving licences are now issued for three years, and the holder is not under an obligation to inform the authorities if he develops epilepsy during that period. There is no legal ruling which governs the issue of driving licences to epileptics in the United Kingdom.

Until about 1948 it was generally held that a person who has at any time suffered from fits should be refused a driving licence (Symonds 1948). The World Health Organisation (1956) recommended that applicants who gave a history of any form of epilepsy should not be permitted to drive. The present tendency is to relax this ruling, but only in respect of private-car drivers. In Britain it is generally held that an epileptic who remains under observation or treatment, and who has been free from attacks for at least three years, may drive a private car, though not public-service or commercial vehicles. The American Medical Association (1959) says that epileptic patients who are not receiving medicaments and who have been free from seizures for at least two years may be allowed to drive private cars but not commercial or passenger vehicles. The Association recommend that such patients should be advised not to take any alcoholic drinks for at least twenty-four hours before driving, and not to drive for more than six hours in any day: driving at night may be dangerous because photic stimuli from opposing headlights may precipitate a seizure, and emotional stress should be minimised by avoiding driving in peak hours. These restrictions probably reflect uncertainty about the safety of such patients as drivers.

In the U.S.A. the present practice varies from State to State.

In eighteen States licences are granted to epileptics on the basis of medical control of seizures; in others an interval of one to three years' freedom is required (Dewey 1955). The State of New York, among others, has laid down a detailed procedure for judging applications (Hilleboe 1959). In Massachusetts (Bonzagni 1954) an applicant who has had epilepsy must present a statement from an approved neurologist, saying that he has been treated, that he has had no seizures for at least eighteen months, and that the physician recommends the issue of a licence. From 1948 to 1954, 512 epileptics applied for licences and 392 were issued on a probationary basis requiring the submission of periodic certificates.

In California, where the procedure is based on a report by Glaser and Irons (1946), epilepsy is a notifiable disease, being defined as "any condition which brings about momentary lapses of consciousness and which may become chronic." All hospitals and many doctors comply with the requirement to notify epilepsy, and about 4000 notifications are received annually. In 1957, licences were withdrawn from 936 drivers because of epilepsy. A further 524 patients who were under treatment at the time of notification were allowed to retain their licences but told to submit medical reports every three to six months. The policy is to require three years' freedom from any lapses of consciousness before a driving licence is restored, but in a cooperative person who has had only a few attacks this period may be reduced to two years. This procedure has been found to work well (James 1958). An obvious difficulty is that compulsory notification may lead to concealment, but California appears to have overcome this.

In 3 London Transport employees an epileptic fit (not while driving) was the first indication that the patient had a carcinoma of the bronchus. As secondaries in the brain may occur in 15% of cases of lung cancer (Simpson 1929), bus drivers who resume work after treatment of this disease are not allowed to continue driving.

Diabetes Mellitus

Patients whose diabetes is controlled by diet alone are considered fit to drive any type of motor vehicle. There is general agreement that those who require insulin, even in small doses, should not drive public-service or heavy commercial vehicles.

Copplestone (1959), in a survey of 56 diabetic drivers who were taking insulin, reported 3 accidents within five years—all in people who said they were not liable to insulin reactions. A controlled study of accident-rates was not possible in this survey. Brandaleone and Friedman (1953) found no excess of accidents among 13 bus operators who were diabetics, but these patients were not receiving insulin.

No comparative studies of accident-rates in diabetic drivers have been made, and there is in any case so much variation between individuals that no safe rule can be laid down. In general, a diabetic receiving insulin is fit to drive a private car if his hypoglycæmic attacks are mild and of slow onset. Rarely, the nature of the attacks changes, and if a patient has sudden or rapid loss of consciousness he should be advised not to drive. The Law has no sympathy for diabetics. The Lord Chief Justice in Armstrong *v.* Clark (1957) stated that insulin is a drug within the meaning of the Road Traffic Act, 1930.

A man of 51 was driving a coach for a provincial company when there was a collision with a van. He was unable to stand without support; a police officer correctly diagnosed hypoglycæmia and administered sugar. This driver had missed his usual meal at 2 P.M. He pleaded guilty to driving under the influence of a drug and was fined, and disqualified for twelve months. He had been treated with insulin for only nine months.

In the early months of insulin treatment, fluctuations and adjustments are to be expected, and during the first year's treatment special care should be given to drivers and the importance and treatment of hypoglycæmic attacks explained to them. Every insulin-treated patient who drives should be made to experience a fairly severe insulin reaction; for otherwise the mild symptoms usually induced at the outset of treatment may give him the impression that insulin reactions are unimportant for him. In these cases the risks arise entirely from treatment.

Complications of diabetes may render a patient unfit to drive, but such complications are considered on their own merits. Thus ocular complications are considered in relation to any defect of vision they may produce. *Renal glycosuria* does not affect driving.

Reactive or functional hypoglycæmia may be of considerable importance.

When there is a quick rise in blood-sugar followed by a rapid fall, the level may occasionally go down to 50 mg., or less, per 100 ml., with actual loss of consciousness. An example in which the patient had an epileptiform attack while in charge of his car is reported by Hay (1958), who thinks that functional

hypoglycæmia probably accounts for some road accidents. Disturbances in behaviour resulting from lesser degrees of hypoglycæmia may be associated with some accidents, but nothing is known about this.

Patients who give evidence of reactive hypoglycæmia should avoid meals consisting almost entirely of carbohydrates. The common present-day habit of going to work fasting, or after a breakfast of toast, marmalade, and sweet tea, may accentuate any tendency to this condition. People who undertake a long drive should have a well-balanced meal beforehand. Hypoglycæmia may be the trigger for an epileptiform attack; and, in any event, people whose consciousness is so labile that they lose it simply by missing breakfast, or through eating a carbohydrate breakfast, should not drive public-service or heavy commercial vehicles. If they appear to understand the condition and act reasonably, they may drive private cars.

Similarly, people whose diabetes is controlled by oral hypoglycæmic agents, such as tolbutamide, may usually be allowed to drive private cars provided they are aware of the possibility of hypoglycæmia. At present it is felt that they should not drive public-service or heavy commercial vehicles, but this view may be modified with experience.

Visual Requirements for Driving

The driver is continually receiving auditory and tactile as well as ocular information, but the ocular information is the most important. The data supplied by a defective ocular apparatus may be incorrect, blurred, incomplete, or delayed.

Several studies have been made in the United States of the relation between visual acuity and accidents.

Lauer et al. (1939), using two different tests of visual acuity, found that higher acuity was associated with fewer accidents. Brody (1941) found that 4 out of 26 accident-repeaters had an acuity lower than 20/30 in the better eye and 20/50 in the worse eye. A comparison of a group of accident-repeaters with a group of accident-free drivers undertaken by the New York Centre for Safety Education indicated that drivers with poor visual acuity are more likely to be involved in accidents than drivers with good acuity (Smeed 1953). Fletcher (1942) found that the proportions of drivers who failed tests of visual acuity were 1% for drivers with good accident records and 5% for drivers with poor records.

These investigations confirm that drivers with poor visual acuity tend to have more accidents than drivers with good acuity; but the point at which impairment of acuity becomes a cause of accidents is unknown. (Perhaps there is no such point, even the slightest impairment increasing accident liability to some extent.) In further studies attention should be paid to different conditions of illumination, which, as Davey (1956) has shown, considerably affect visual acuity. This is illustrated in table IX.

14 drivers aged 50–65 were tested on Snellen's types indoors, with an illumination of 35 lumens on the test chart and immediately afterwards out of doors in June and July, 1958, in conditions varying from cloudy to bright sunshine (table IX). In the stronger light outdoors, 1 of the 28 eyes improved in visual acuity from 6/60 to 6/12 and 10 improved at least three lines on the test chart; all 28 improved at least one line. Visual efficiency increases with higher illumination, but the improvement in acuity shown by these men is largely due to reduction in the size of the pupil. No quantitative relation is to be expected; for age, pigmentation, refractive error, and emotional state all affect the reaction of the pupil to changes in retinal illumination.

TABLE IX—RESULTS OF VISUAL ACUITY (SNELLEN) TESTS ON 14 DRIVERS UNDER DIFFERENT CONDITIONS OF ILLUMINATION

Indoor reading (35 lumens on chart)	No. of eyes	Outdoor reading		
6/60	5	6/24 (2)	6/18 (2)	6/12 (1)
6/36	7	6/18 (3)	6/12 (3)	6/9 (1)
6/24	2	6/12 (2)		
6/18	3	6/9 (1)	6/6 (2)	
6/12	5	6/9 (2)	6/5 (3)	
6/9	3	6/6 (1)	6/5 (2)	
6/6	3	6/5 (3)		

At night a driver's visual acuity may be worsened by this intrinsic factor as well as by reduced visibility.

Smeed (1953) studied the changes in adult pedestrian casualties which occurred when summertime was introduced and removed. He found that in the hours that change from light to dark the number of casualties was approximately doubled, while in those that change from dark to light the number was halved. There appeared to be no changes in traffic density which could explain these findings.

One main problem at night is that of dazzle, and Savin et al. (1957) point out that " dark glasses can help against dazzle, but at the expense of lowering general visibility ". It cannot be too strongly emphasised that any coloured glass in front of the eyes—spectacles, a tinted windscreen, or an anti-dazzle visor—is an obstruction to the driver's vision and should not be used at night. Under simulated night-driving conditions, with glare, Miles (1955) measured the effect of tinted glass on the visual acuity of subjects having normal daylight vision. Tinted glass, of all colours, always reduced visual acuity, the reduction being less in subjects who complained of glare than in those who did not. Yellow-tinted glass makes some drivers think that the visual field is brighter, but this impression is false: such glass adversely affects their visual efficiency, especially at night. Yellow-tinted lenses are particularly disadvantageous to colour defectives (Miles 1954). A clear-glass windscreen transmits about 92% of the light falling on it, while the lightest yellow filter passes only about 88%. A combination of the two passes only about 81% under ideal conditions and considerably less when it is dirty or scratched (*British Medical Journal* 1954). The many problems of vision in relation to driving were discussed by Kelly et al. (1955), with bibliography.

In the absence of a precise method of relating visual acuity to the requirements of driving, various arbitrary standards have been recommended. The American Medical Association (1959) regards a corrected vision of 20/40 as adequate for driving a private vehicle; those with vision less than 20/40 should be referred to an ophthalmologist. At present there is no uniformity of opinion about visual acuity between 20/40 and 20/70. Patients with less than 20/70 corrected vision in the better eye should be advised not to drive. The British Medical Association (1954) recommends that drivers of public-service and heavy vehicles should have a minimum corrected visual acuity of 6/9 in one eye and 6/24 in the other, but makes no recommendation for private-vehicle drivers. The World Health Organisation (1956) says that drivers of heavy vehicles should have a corrected visual acuity of at least 1·6 for both eyes together; for drivers of light vehicles (including private cars) their minimum is 0·8.

Davey (1958) recorded the visual acuity of 1534 private-car drivers who consulted opticians in this country because of difficulty in seeing (often presbyopia). 5 drivers had a binocular corrected visual acuity lower than 6/18—worse, that is, than the " number plate reading at 25 yards " standard required for the issue of a

driving licence. (This corresponds to a visual acuity of about 6/15.) Of those who sometimes drove without using their spectacles, 26 had an uncorrected visual acuity below the driving-licence standard.

No data are available for the accident experience of one-eyed drivers. Many one-eyed persons acquire judgment of distance and develop the ability to drive private cars safely; they should not be employed to drive public-service or heavy vehicles. The ability to see with both eyes together at the same time is a visual characteristic of accident-free drivers more than of accident-repeaters (Eno Foundation 1948). Schwartz (1939) found that one-eyed drivers had a higher prevalence of accidents at intersections, and that these accidents were often on the side *away* from the defective eye. Apparently the driver turns his head to compensate for the loss of visual field on his blind side.

Cole (1959) found that 5·27% of patients referred for sight-testing had unilateral amblyopia, and this condition may be of some importance in relation to road accidents. Objects approaching from the amblyopic side tend not to be seen until they come within the visual field of the good eye. There is no reason to prevent people who have unilateral amblyopia from driving their own cars, but they should be made aware of this minor defect and how it affects their vision.

The visual fields are as important for safe driving as visual acuity. Visual form fields of 140° are sufficient for operating a motor vehicle, but fields less than 110° are not. The patient with a field between these limits should be assessed on the basis of the conditions under which he drives and the amount of lateral vision he possesses (American Medical Association 1959).

The importance of depth perception, dark adaptation, and ocular muscle imbalance has not been elucidated and it is usual to ignore these qualities in relation to driving, except where muscle imbalance produces uncontrolled diplopia: such patients should be advised not to drive.

Colour vision

There has been no evidence of any relation between accidents and defective colour vision. Nevertheless, definite opinions have been expressed. Strong (1955), in discussing fitness to drive private cars, stated that "accurate colour perception must be shown"; but this would exclude about 8% of the male population from driving at all. More recently it has been said that defective colour vision is not associated with accidents (World Health Organisation 1956, American Medical Association 1959).

The problem of colour-defective drivers was therefore studied in London Transport.

149 Central Bus drivers have been found who have defective colour vision; they made numerous errors on both the Ishihara test and the Edridge-Green lantern test. These men were recruited as drivers before colour-vision tests were employed, and all of them have more than fifteen years' service. 149 drivers were selected as controls, each matched with a colour-defective driver for age and length of service. Each colour-defective driver and his control worked at the same garage and on the same routes. The controls all had normal colour vision. The accident experience of these two groups of drivers was then compared. Each group covered approximately 4200 driver-years, an average of 25·7 years' service per driver. For the purposes of this study, every entry of a blameworthy accident in the driver's staff record has been included. The definition of an "accident" is therefore the same in the colour-defective and control groups, and as each colour-defective driver and his control worked at the same garage, there should be no administrative difference between the two groups in the recording of accidents. The great majority of accidents were minor collisions. The results of this investigation are shown in table x.

TABLE X—L.T. CENTRAL BUS DRIVERS: ACCIDENTS EXPERIENCED BY COLOUR-DEFECTIVES AND CONTROLS

—	Colour-defective			Not colour-defective
	More severely defective	Less severely defective	Total colour-defective	
Drivers	76	73	149	149
Accidents	327	354	681	712

The colour-defective drivers experienced 681 accidents and the control group 712: thus there is no significant difference in the accident experience of the two groups. The colour-defective drivers were divided into a group of 76 with more severe colour defect and 73 with less severe. Again there is little difference between the two groups; the severely defective experienced 327 and the less severely defective 354 accidents.

13 colour-defective drivers and 11 controls were found guilty of failing to conform with traffic-light signals; other traffic offences amounted to 13 in the colour-defective group and 15 in the controls. Special observation of 6 colour-defective drivers, 4 of them in the "more severe" group, including observation at night, revealed that all of them negotiated traffic lights promptly and correctly. The record of one driver is of interest. In 1932 it was recommended that, because of his severely defective colour vision, he should not be employed where traffic lights operate. This recommendation could not be carried out, and in 1957 he was given the safe driving award for twenty-five years' driving without a blameworthy accident.

This study showed conclusively that colour-defective bus drivers did not have more accidents than the normally sighted. These men, however, are professional drivers who practise their skill for several hours on every working day of their lives. It remains possible that the experience of those who drive only occasionally might be different.

Impairment of Hearing

There are no generally accepted standards of hearing for drivers, and information about the safety or otherwise of deaf drivers is surprisingly scarce. An inquiry some years ago ("Rex" 1953) showed that some insurance companies do not grant policies to deaf drivers, but the majority are willing to consider each case on its merits. The same paper refers to a study suggesting that there is little difference between the accident-liability of the deaf and those with normal hearing: in fact, the investigation showed a slight balance in favour of the deaf, which was explained by their exercising extra care. Macfarlan (1937) said that the deaf are generally safe drivers: they are cautious and on the alert because they know the risk they are taking.

While good hearing is an undoubted asset to a driver, it is by no means essential. In some cases hearing may be more acute in the noise of traffic than in a quiet room; it is doubtful whether driving safety is materially enhanced by high degrees of auditory perception such as are required to hear a whispered voice at a considerable distance in a still room. For hearing an overtaking vehicle, hearing in the right ear is sometimes said to be more important in countries where vehicles are driven on the left side of the road; but deafness on either side will hinder location of a sound. In a competent and experienced driver moderate impairment of hearing is unlikely to detract seriously from driving ability. No benefit is to be expected from the use of hearing-aids—because of extraneous noises, variability,

and mechanical defects which may develop in the instrument, and because of difficulty in locating the sound. On the whole they are better not used while driving.

Persons who apply for the first time for a permit to drive public-service or heavy commercial vehicles should not be allowed to undertake this work if their hearing is impaired in more than a minor degree. In the trained, experienced driver deafness need not be a bar to driving unless it is severe enough to interfere with performance of the work.

Conclusion

In people who have multiple disabilities the assessment of fitness to drive may be difficult; but in general the effects of such disabilities are additive. Physical handicaps, such as the loss of a limb, are seldom a bar to driving a private car, which can be specially adapted if necessary; but men with more than a minor loss of function in a limb should not be employed as drivers of public-service or heavy commercial vehicles. The cumulative effects of ageing and minor disabilities may reach a stage at which the elderly should be advised to discontinue driving: indeed this may be necessary in the absence of any clearly defined disability.

While some doctors can contribute to road safety by working in research teams, a great many can do so by advising patients on the effects of disabilities, diseases, and drugs.

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EXTRACTION OF A GASTRIN-LIKE SUBSTANCE FROM A PANCREATIC TUMOUR IN A CASE OF ZOLLINGER-ELLISON SYNDROME

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EXPERIMENTAL diversion of pancreatic juice from the duodenum of conscious dogs is often followed by peptic ulceration of the duodenum (Matthews and Dragstedt 1932); but ulceration rarely follows total pancreatectomy (Berg 1934). These observations prompted the suggestion (Poth et al. 1948) that pancreatic islet cells might produce an ulcerogenic agent; and later two cases were reported of non-insulin-secreting islet-cell adenomata associated with gastric hypersecretion and peptic ulceration of the jejunum (Zollinger and Ellison 1955).

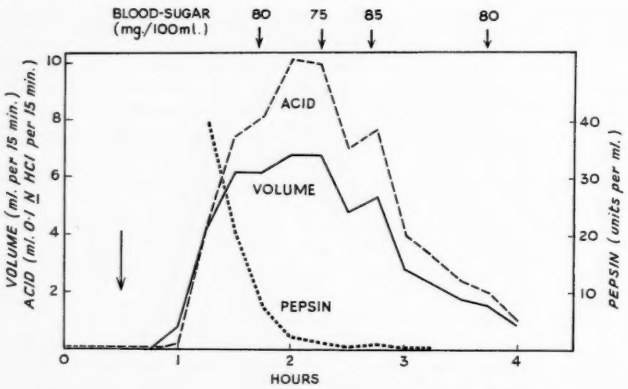

Fig. 1 (dog no. 1)—Response of the denervated fundic pouch to the subcutaneous injection of the first tumour extract (at 30 minutes). Blood-sugar values at times indicated by arrows.

In the last 5 years more than a hundred cases of the "Zollinger-Ellison syndrome" have been recorded. However, in no case so far reported has gastric secretion been studied on the intact stomach before and after removal of a pancreatic tumour; and apparently no attempt has been made to extract from such a tumour a substance capable of stimulating gastric secretion.

The observations reported here were made on a tumour of the pancreas removed by Prof. F. A. R. Stammers from a case of the Zollinger-Ellison syndrome admitted to the medical unit of the Queen Elizabeth Hospital, Birmingham. Full details of the case, and the clinical and pathological investigations, will be reported separately (French and Stammers 1960). The present communication is concerned with the biochemical and physiological investigations on the tumour.

The patient, a man aged 55, presented with episodic dyspepsia and diarrhœa and was found to have a duodenal ulcer, œsophagitis, and steatorrhœa. Basal and nocturnal gastric acid secretions were found to be elevated to levels commonly associated with the Zollinger-Ellison syndrome, and the pH of secretions aspirated from the distal duodenum frequently lay between 1·0 and 1·5. A presumptive diagnosis of the Zollinger-Ellison syndrome led to laparotomy, and a small tumour attached to the head of the pancreas was found and removed. No other surgical procedure was carried out. The patient became free of symptoms from the first postoperative day.

Immediately after removal, two-thirds of the tumour (about 2 g.) was cooled to −70°C, and thereafter it was kept deeply frozen until used for the investigations described below. The remaining third was examined histologically and found to be an islet-cell neoplasm.

Experimental

In collaboration with Prof. W. L. M. Perry and Dr. H. M. Adams of the department of pharmacology, University of Edinburgh, a simple extract was made from 600 mg. of the tumour by homogenisation in Tyrode's solution. The histamine activity of the homogenate was found to be less than 0·25 μg. base per gramme of fresh tissue. Varying amounts of this extract were infused into the anæsthetised rat preparation of Ghosh and Schild (1958) and injected intravenously into a conscious Heidenhain-pouch dog. No evidence was obtained of the presence in the extract of a stimulant of gastric secretion, and no pyrogenic or other toxic effects were observed.

It was argued that if the tumour did in fact contain a stimulant of gastric secretion, this might be similar in chemical nature to the antral hormone gastrin, since, in order to enter the general circulation and so cause the gastric hypersecretion observed clinically, it must first survive passage through the liver, as does gastrin. It was therefore agreed to extract a portion of the tumour by a method shown to be successful for the preparation from hog antral mucosa of the hormone gastrin. Another portion of the tumour, weighing 800 mg. was accordingly thawed, minced finely with rather more than its own weight of moist picric acid crystals, and sent by post to Liverpool for further treatment.

The method used was adapted from that recently evolved by Gregory and Tracy (1959) for the extraction of gastrin from hog antral mucosa.

This method (soon to be published in full) provides an extract which is free from histamine, but which, like the antral hormone, stimulates the secretion of gastric acid, but not of pepsin. The extract, in contrast to those hitherto described, has been found effective when injected subcutaneously into conscious dogs, as well as intramuscularly or intravenously.

The method commences with treatment of the fresh tissue with picric acid; and it has been found (Gregory and Tracy, unpublished) that at this stage gastrin activity survives for some days at least under conditions of simple refrigeration or even at room temperature. In the present instance this fact was of great advantage, since it made possible convenient transport of the tissue without loss of activity.

The mixture of tumour and picric acid was ground with fine sand and then extracted overnight at room temperature with

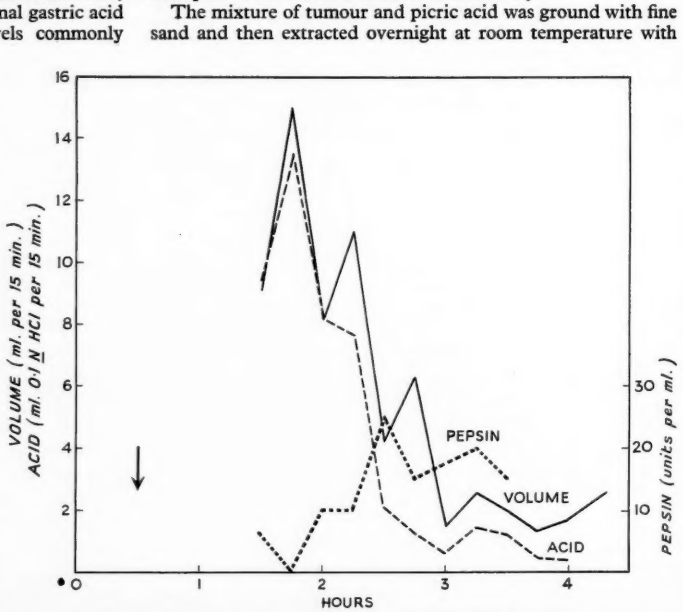

Fig. 2 (dog no. 1)—Response of the main stomach (gastric fistula) to the subcutaneous injection of the first tumour extract (at 30 mins.). Samples before 90 minutes lost. Same experiment as in fig. 1.

an excess of acid aqueous acetone. The acetone and acid were removed and the aqueous residue precipitated and washed with trichloracetic acid solution. The precipitate was then dissolved and inert protein removed. The final product was a clear solution (5 ml.) having a pH of 8·2, in approximately 0·9% NaCl solution.

This extract was given as a single subcutaneous injection to a fasting conscious dog (dog no. 1) provided with a gastric fistula and also a completely denervated fundic pouch (Gregory 1958). After about 15 minutes there ensued a large and prolonged secretory response from the pouch (fig. 1). The main stomach also secreted, though to a lesser degree, having regard to the relative size of the stomach and the pouch (fig. 2). This disparity between the main stomach and the pouch was also shown by this dog in response to injections of gastrin and of histamine, and is probably attributable to the fact that

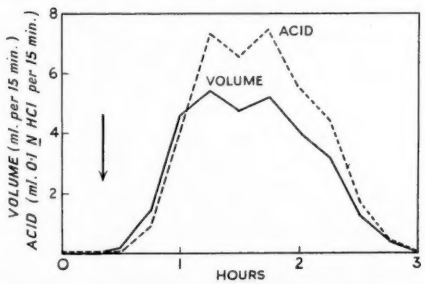

Fig. 3 (dog no. 1)—Response of the denervated fundic pouch to the subcutaneous injection of a gastrin extract equivalent to 20 g. fresh hog antral mucosa (at 20 minutes).

the gastric fistula had been prepared more recently than the pouch.

The total amount of acid secreted by the pouch in response to the tumour extract, during the 210 minutes for which secretion lasted, was 6·71 mEq. HCl. There was no stimulation of pepsin secretion in either the pouch or the main stomach, and the animal's blood-sugar remained unchanged. There were no effects on respiration, heart-rate, or general behaviour.

The response of the denervated pouch in the same dog to a subcutaneous injection of gastrin equivalent to 20 g. of fresh hog antral mucosa, prepared by the method on which the extraction procedure used for the tumour was based, is shown in fig. 3. The total amount of acid secreted by the pouch was 3·73 mEq. HCl; so that, comparing the responses, the tumour was 45 times as active in stimulating secretion as an equal weight of hog antral mucosa. The reponses shown to gastrin and to the tumour extract, both by the pouch and the main stomach, were closely similar, and quite different in pattern from the response of the same dog to a subcutaneous injection of 1 mg. histamine acid phosphate (fig. 4).

In the same dog, the subcutaneous injection of 20 units of soluble insulin caused a considerable secretion of acid and pepsin from the main stomach, but no detectable response from the denervated pouch (fig. 5). This, together with the fact that the blood-sugar level did not change after injection of the tumour extract, excludes any possibility that its effect on the pouch was due to the presence of insulin.

The remainder of the tumour (425 mg.) was now treated with picric acid and despatched as before; on arrival in Liverpool it was extracted in precisely the same manner as the first portion. One-tenth of the final solution (0·5 ml., corresponding to 42·5 mg. fresh tissue) was set aside for testing on the blood-pressure of the anæsthetised cat; the remainder was injected subcutaneously into a dog (dog no. 2) different from the one previously used. This animal was provided only with a denervated fundic pouch. The extract was injected subcutaneously at two sites. There followed a considerable secretory response, which was of more prompt onset (less than 15 minutes) but more prolonged, than in the first dog (fig. 6); the total amount of acid secreted during the 285 minutes for which the response continued was 3·2 mEq. HCl. The undulatory character of the response is probably attributable to some variation in the rate of absorption from the two sites of injection. As before, there were no side-effects.

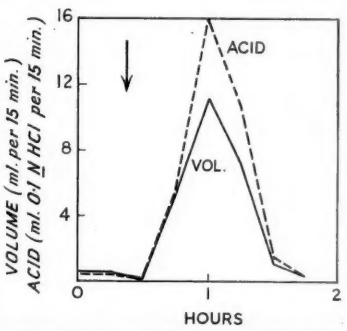

Fig. 4 (dog no. 1)—Response of the denervated fundic pouch to the subcutaneous injection of 1 mg. histamine acid phosphate (at 20 minutes).

On another occasion, this dog was injected subcutaneously with the same amount of the same gastrin preparation as had been given to the first dog; it secreted a total of 4·87 mEq. HCl. Comparing these responses, the tumour was 33 times as active in stimulating secretion as an equal weight of hog antral mucosa. This is in reasonable agreement with the factor of 45 calculated on the basis of the first experiment in dog no. 1.

That the effect of the extract was unlikely to be due to the presence of histamine seemed clear from (1) the negligible histamine activity of the simple saline homogenate originally made, (2) the fact that the extraction procedure used involved precipitation and washing with trichloracetic acid, and (3) the difference in form of the secretory response to the tumour extract and that produced by histamine in the same dog. Nevertheless, the aliquot of the extract which had been saved was diluted with an equal volume of 0·9% NaCl solution and used

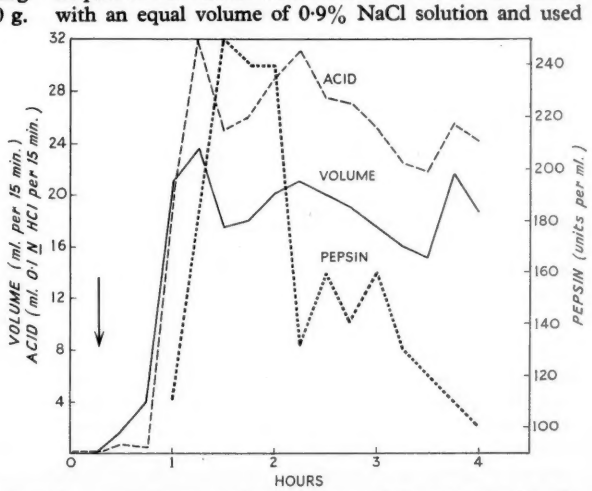

Fig. 5 (dog no. 1)—Response of the main stomach (gastric fistula) to the subcutaneous injection of 20 units soluble insulin (at 15 minutes). The denervated fundic pouch did not secrete.

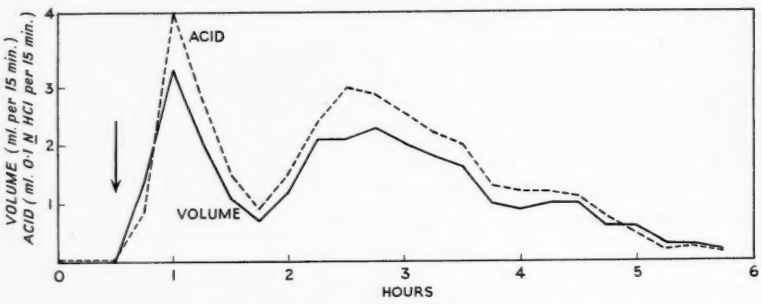

Fig. 6 (dog no. 2)—Response of the denervated fundic pouch to the subcutaneous injection (at 30 minutes) of the second tumour extract.

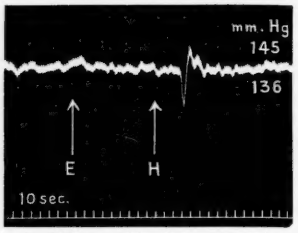

Fig. 7—Effect on blood-pressure of an anæsthetised cat of intravenous injection (at E) of an aliquot of the second tumour extract equivalent to about 20 mg. fresh tissue. At H, intravenous injection of 0·25 μg. histamine base.

for two intravenous injections into an anæsthetised cat (fig. 7). There was no significant vasodilator effect, whereas a similar injection of 0·25 μg. of histamine base caused the usual sharp and considerable fall in blood-pressure. Thus the extract contained no detectable amount of histamine, nor did it cause the release of histamine on intravenous injection.

Discussion

These experiments establish that the tumour extract contained a substance which in its chemical and physiological properties resembled the antral hormone gastrin. Its activity was not due to histamine or insulin; nor did it cause the release of histamine on intravenous injection. The amount of gastrin-like activity found in the tumour was many times greater than that which can be extracted from fresh hog antral mucosa by the method on which the procedure used for the tumour was based.

The present findings do not establish that the active principle in the tumour extract was in fact gastrin; but they do establish that it must have been a substance of similar chemical nature, and that its effects on the secretion of gastric acid and pepsin were identical with those shown by gastrin in similar circumstances. The amount of tissue available was too small for any further comparison between the chemical properties of the active principle and that of gastrin; but this might be possible in the future.

One question which obviously arises is whether normal pancreas contains a similar gastrin-like substance. The method described has not been applied to normal human pancreas; but Gregory and Tracy (unpublished) have not succeeded in extracting any such activity from fresh hog pancreas.

So that examination of similar tumours in the future shall be as fruitful as possible, it seems worth emphasising (*a*) that attempts to demonstrate secretogogue activity in simple saline extracts are unlikely to succeed, and (*b*) that the activity survives at least several days, even at room temperature, once the fresh tissue has been thoroughly impregnated with picric acid.

Conclusion

The pancreatic tumour from a patient with the Zollinger-Ellison syndrome has been shown to contain large amounts of a substance which in its chemical and physiological properties resembles the antral hormone gastrin.

Two preparations made from the tumour by a method which extracts gastrin from hog antral mucosa stimulated the secretion of gastric acid, but not of pepsin, when injected subcutaneously into conscious dogs.

The activity of the preparations was not due to the presence of insulin or histamine.

We wish to thank Prof. W. L. M. Perry and Dr. H. M. Adams of the department of pharmacology, University of Edinburgh, for their kind assistance with the initial treatment of the tumour.

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FATTY FOODS AND OBESITY

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IN several recent reports a diet containing much fat but little carbohydrate has been advocated for reducing the weight of obese patients. This principle is not new; it was mentioned in 1932 by Lyon and Dunlop, and later by Pennington (1954). But not until Kekwick and Pawan's experimental studies (1956) were published did the high-fat reducing diet begin to attract attention in the popular press in Britain and Scandinavia (Mackarness 1958).

The suggestion was that if the diet is sufficiently low in carbohydrate (less than 60 g. a day), the obese patient will lose weight even if the calorie intake considerably exceeds that of the composite diet on which he had previously remained overweight. This can of course only be true if the fatty food is capable of augmenting energy expenditure. Kekwick and Pawan (1956), whose conclusions were far more guarded than those of their journalistic followers, accepted the existence of such a " luxury consumption ", believing that energy expenditure is increased by proteins and especially by fats, whereas it is decreased by carbohydrates. The crucial point of their work was the observation that four out of five obese patients lost 1–2·6 kg. when, for a week, a normal composite diet of 2000 calories was replaced by a diet of 2600 calories given mainly as fat and protein. In another experiment fourteen obese patients were given, in successive weeks, three different diets, each of 1000 calories, of which carbohydrate, protein, or fat comprised 90%. Most weight was lost with the high-fat diet; the high-protein diet was somewhat less effective; and little or no weight was lost on the high-carbohydrate regimen.

When we planned the following study, it was clear that some of the questions raised by reports on the effect of a fatty diet did not require new experimental studies, because they could be answered by generally accepted

physiological facts. Classical reports on the specific-dynamic action of foodstuffs do not point to any increase of metabolism due to fat; on the contrary, the action of fat seems to be smaller than that of carbohydrate, and this has recently been confirmed by Hawthorne et al. (1956). Swift et al. (1959) found no appreciable difference in the energy utilisation by man of equicaloric diets containing widely different amounts of fat. We know, moreover, that an intact digestive canal absorbs large quantities of fat as effectively as it does normal amounts. This leaves the possibility that the weight fluctuations observed by Kekwick and Pawan (1956) are due to alterations in the body's fluid content. Kekwick and Pawan tried to check this possibility by determining total body-water, and they found that the ratio body-weight/body-water remained remarkably constant during weight loss on the various diets.

The fact that some of Kekwick and Pawan's obese patients temporarily maintained their weights on high carbohydrate diets yielding as little as 1000 calories (which is decidedly lower than the basal metabolism of a euthyroid adult) while others lost weight on high-fat diets containing as much as 2600 calories, seems to us to be the best indirect argument against Kekwick and Pawan's main premise—namely, that the proportion of water in body-weight is unchanged. Their data reveal, not surprisingly, that some patients lost considerably less water than the average 30–50% of the weight loss, while others augmented their total body-water content despite weight losses of up to 3·6 kg. In some the loss of water was much greater than the average, and in a few the water loss exceeded the loss of body-weight. This can only mean that the method of determining total body-water was too inaccurate to allow safe conclusions regarding fluctuations in body-fluid during short observation periods.

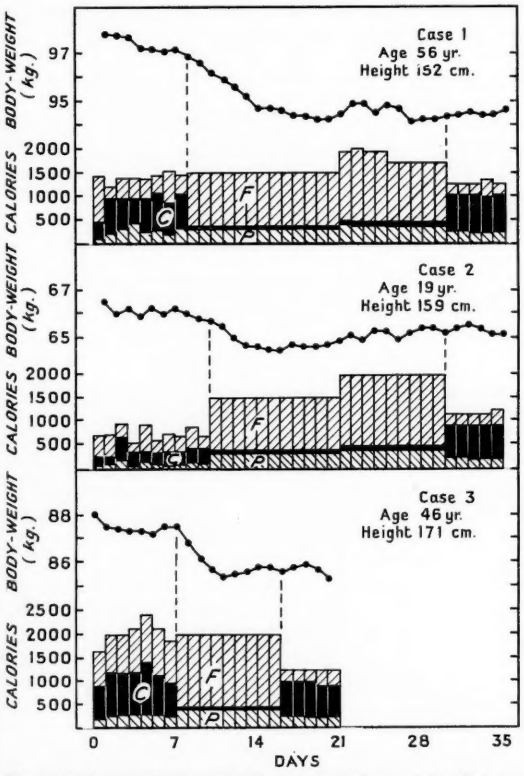

Fig. 1—Body-weight of cases 1–3 on a normal composite diet, on a high-fat/low-carbohydrate diet (1500–2000 calories), and on a high-carbohydrate/low-calorie diet.
F = fat; C = carbohydrate; P = protein.

The Investigation

We studied eight female volunteers, with various degrees of obesity but no other disorder thought to be relevant.

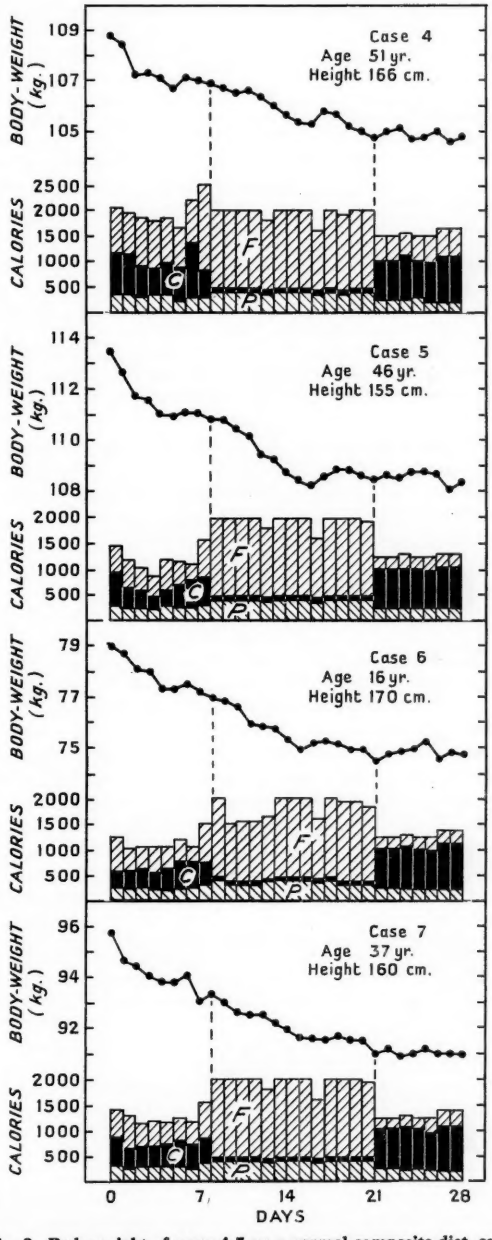

Fig. 2—Body-weight of cases 4–7 on a normal composite diet, on a high-fat/low carbohydrate diet (about 2000 calories), and on a high-carbohydrate/low-calorie diet.
F = fat; C = carbohydrate; P = protein.

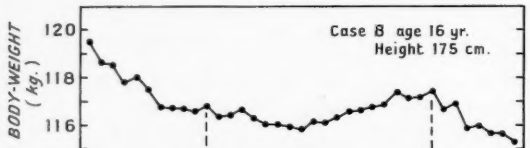

Fig. 3—Body-weight of case 8 on a normal composite diet, on a high-fat/low-carbohydrate diet (2600 calories), and on a high-carbohydrate/low-calorie diet.
F = fat; C = carbohydrate; P = protein.

The patients remained in hospital under strict control throughout the observation period, but they were not kept in bed. They were weighed at the same time every morning, fasting and naked, after they had passed water but not defæcated. For the first few days we gave them ordinary composite food ad libitum. The meals were prepared in a special kitchen from weighed ingredients; the individual helpings and what might be left over were weighed, and the intake was calculated in terms of calories, protein, fat, and carbohydrate.

Their spontaneous food intake was considerably smaller than that regarded as necessary for maintaining energy balance. The initial weight-loss subsided after 5–8 days, and body-weight was tolerably stable when we altered the diet (fig. 1).

We next gave them less than 25 g. of carbohydrate daily, the rest of the calories being divided between protein and fat in the proportion of about 1/5. Of this fatty diet the first two patients (cases 1 and 2) consumed 1500 calories daily. For case 1 this corresponded to the spontaneous intake in the initial period. Their weights decreased during the next 5–7 days, and then they again stabilised themselves. During the next 9 days, when the patients had an intake of about 2000 calories from the high-fat diet, case 2 gained about 1 kg. while the weight of case 1 did not change significantly. The third patient (case 3) was given a 2000-calorie high-fat diet directly after the free-fare period, corresponding to her initial spontaneous calorie intake; she too had a striking loss of weight during the first 5 days and then her weight stabilised itself.

A similar pattern was found in the next four patients (cases 4–7) who, for 13 days, took about 2000 calories daily as a fatty diet (fig. 2).

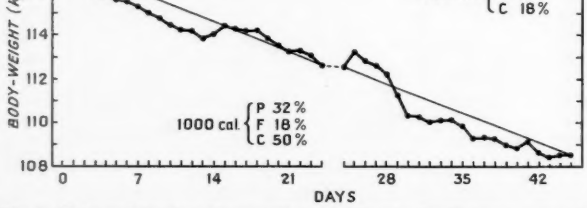

Fig. 4—Body-weight of an obese patient (case 8), who for 45 days consumed 1000 calories a day—as a carbohydrate/low-fat diet during the first 24 days, and as a low-carbohydrate/high-fat diet during the last 21 days.
F = fat; C = carbohydrate; P = protein.

During the last 5–7 days of the observation period all seven patients had about 1250 calories daily in the form of a diet relatively high in carbohydrate (about 60% of the calories), and all their weights remained practically unaltered. Their basal metabolic rates showed that this calorie intake was less than their minimum energy requirements, and it must therefore be assumed that they had drawn on their energy stores during this period. The fact that their weights were unchanged can only be explained by water retention—possibly connected with glycogen storage. Our 1250-calorie diet was only relatively rich in carbohydrate, containing if anything less carbohydrate than normal food. If, as we think is inevitable, one assumes that our patients retained water on this moderate carbohydrate intake, then it must follow that they were in a state of relative dehydration during the preceding period. The weight loss during the first 5–7 days of the fatty diet seems to reflect this dehydration. Thus the initial weight loss associated with the high-fat diet is not, in our opinion, due to a reduction of the fat deposits, and it cannot be termed "slimming" in the accepted sense of this word.

OXYGEN CONSUMPTION DURING REST AND DURING STANDARDISED MUSCULAR EXERTION ON A NORMAL COMPOSITE DIET, AND ON A HIGH-FAT/LOW-CARBOHYDRATE DIET

Case no.	Diet	Metabolism (calories per min.)		Ratio: Metabolic increase (calories per min.)
		At rest	At work	Body-weight (kg.)
1	Normal	1·18	3·54	0·026
	,,	0·95	3·51	0·028
	Fatty	1·16	3·53	0·025
	,,	1·02	3·55	0·027
	,,	1·10	3·71	0·028
2	Normal	1·02	2·82	0·028
	,,	0·93	2·58	0·025
	Fatty	0·92	2·47	0·024
	,,	0·98	2·31	0·020
	,,	0·89	2·30	0·022
3	Normal	1·15	3·20	0·023
	Fatty	1·09	3·38	0·026
	,,	1·16	3·20	0·024
4	Normal	1·07	3·47	0·022
	Fatty	1·20	4·00	0·026
5	Normal	1·27	5·05	0·033
	Fatty	1·42	4·44	0·028
6	Normal	1·26	3·38	0·027
	Fatty	1·20	3·02	0·024
7	Normal	1·26	4·12	0·030
	Fatty	1·15	3·90	0·030
8	Normal	1·29	4·52	0·028
	Fatty	1·44	4·52	0·027
Average	Normal	1·14	3·62	0·027
	Fatty	1·13	3·42	0·026

Our last patient (case 8, fig. 3) was the only one able to consume as much fatty food (2600 calories a day) as was given by Kekwick and Pawan (1956). For 19 days she took this diet, which contained 40 g. of carbohydrate. Like the other patients she lost weight during the first week and then she began to gain. This was hardly surprising considering the calorie value of the food, and the increase in weight must have been due to deposition of fat. She was afterwards given 1000 calories a day of a diet relatively high in carbohydrate (50%), and her weight began to decrease. The reason she did not maintain her weight like the other patients

during this stage of the experiment, seems to be that her calorie deficit was too great to permit glycogen deposition and rehydration.

To throw light on whether a fatty diet poor in calories causes more weight to be lost than an equicaloric high-carbohydrate diet, we gave case 8 1000 calories (32% protein) daily for 45 days, with 50% carbohydrate and 18% fat during the first 24 days, and 18% carbohydrate and 50% fat during the last 21 days (fig. 4). The weight curve wavered somewhat, but not systematically, and on each diet the weight loss after 21 days was exactly the same—namely, 4·1 kg.

Discussion

Our patients are too few to allow far-reaching conclusions; but all the same we believe that our observations do carry certain weight, partly because of their uniformity and partly because our observation periods were longer than those of Kekwick and Pawan (1956).

Our dietary experiments were supplemented with determinations of oxygen consumption during the periods of ad-libitum and of fatty diet. Energy metabolism was computed as calories per minute, and determinations were made 3 hours after breakfast, first during rest and then during standardised muscular exertion which comprised stepping on and off a small stool at a fixed pace (table I). As might be expected, the figures vary from one determination to another, but they do not support the assumption that energy expenditure is higher on a fatty diet than on a normal food intake. Because muscular exertion must vary with the body-weight at least, we divided the metabolic increase by the weight of the patient (right-hand column). The figure thus obtained does not vary appreciably for each patient, and it is of the same magnitude for the whole group.

We should perhaps point out that this study does not answer the question of whether a high proportion of fat makes it easier for obese patients to restrict their calorie intake.

Summary

Eight obese women were treated in hospital with the following successive diets:

1. Plain composite food ad libitum for 7–10 days.
2. A diet with a high-fat content, yielding 1500–2600 calories, and a carbohydrate content of 25–40 g. for 9–22 days.
3. A diet of low-calorie value (about 1250) but of comparatively high carbohydrate content for 5–7 days.

We were led to the following conclusions:

1. A high-fat/low-carbohydrate diet may reduce the weight of obese people considerably. But this weight-loss ceases after a few days and it may be explained largely—perhaps wholly—by release of water from deposits in the body.
2. Continued intake of a high-fat/low-carbohydrate diet affects body-weight in the way expected from the number of calories ingested.
3. A diet containing a relatively high proportion of carbohydrate, but with a calorie intake below the theoretical minimum, may be compatible with a stable body-weight—at any rate if taken after a period of fatty diet. This is most likely attributable to simultaneous increase of the body's fluid content.
4. In a single experiment such a high-carbohydrate diet, continued for 3 weeks, produced a loss of weight which was identical with that produced, during the next 3 weeks, by an equicaloric high-fat diet.
5. The oxygen consumption of our obese patients, measured during rest and during standardised exertion, was no higher on a fatty diet than on an ordinary composite diet.

References at foot of next column

CARBON-MONOXIDE DIFFUSION
SIMPLE TEST FOR ROUTINE CLINICAL USE

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DIFFUSION of oxygen from alveolus to pulmonary capillary is increasingly often measured by carbon-monoxide-diffusion tests in respiratory and cardiac disease; but, because the equipment is expensive and the tests are complex, these have so far been practicable only in specially equipped laboratories (Simpson 1959).

The test described here is suitable for use in any hospital laboratory or at the bedside.

Apparatus

The apparatus consists of (*a*) two Douglas bags connected via a one-way valve so that the subject inhales from one and exhales into the other; and (*b*) a carbon-monoxide analyser (fig. 1).

This is a palladosulphite carbon-monoxide detector (marketed by Siebe, Gorman & Co., Ltd., of Chessington, Surrey) comprising a simple aspirator pump for drawing the gas under test through an indicator tube, which contains silica crystals impregnated with potassium palladosulphite, which changes colour from an initial light yellow to a distinctive brown in the presence of carbon monoxide. The carbon-monoxide concentration is indicated by the length of brown stain produced, and is read from a calibrated chart. The expendable tubes cost 3*s*. 9*d*. each.

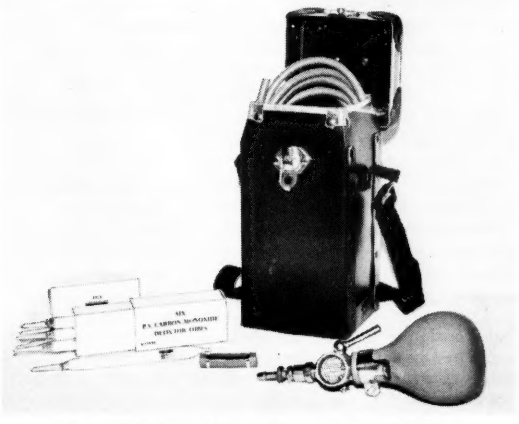

Fig. 1—Palladosulphite carbon-monoxide detector.

Procedure

The " inhale " Douglas bag is charged with about 50 litres of air or oxygen plus about 20 ml. pure carbon monoxide or about 130 ml. of coal gas, giving a carbon-monoxide concentration of approximately 0·04%.

As the palladosulphite analyser has been developed for use with coal gas, this can be used as a source of carbon monoxide, and the taste and smell at such a concentration are hardly noticeable.

DR. OLESEN, DR. QUAADE : REFERENCES

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TABLE I—ESTIMATES OF CARBON-MONOXIDE CONTENT (%) OF VARIOUS GAS MIXTURES BY MEANS OF PALLADOSULPHITE ANALYSER COMPARED WITH RESULTS BY MEANS OF INFRA-RED ANALYSER

Reading from infra-red analyser	Palladosulphite analyser		
	Reading	Error	% error
0·026	0·0275	+0·0015	+ 6%
0·026	0·025	−0·001	− 4%
0·0386	0·035	−0·0032	− 9%
0·0386	0·035	−0·0032	− 9%
0·035	0·035	Nil	Nil
0·016	0·018	+0·002	+12%
0·045	0·049	+0·004	+ 9%
0·0184	0·017	−0·0014	− 8%
0·044	0·044	Nil	Nil
0·0177	0·017	−0·0007	− 4%

The patient starts to breathe the mixture, and the gas is sampled via the side tube of the bag. At the end of one minute the taps of the bags are turned off, and the expired gas is sampled. Finally the gas from the " expire " bag is run through a gasometer to give the minute volume, should this measure be required.

The carbon monoxide extracted, which is the difference between the concentration of inhaled and of exhaled gas, is expressed as a percentage of the inhaled gas carbon-monoxide concentration:

$$\text{Carbon-monoxide \% extraction} = \frac{\text{inhaled carbon-monoxide content minus exhaled carbon-monoxide content}}{\text{inhaled carbon-monoxide content}} \times 100$$

The test can easily be repeated, and duplicate estimations are probably advisable.

Assessment of Accuracy

Great care must be taken in reading the length of stain, and the criteria of stain length must be kept constant.

Four readings are taken round the circumference of the tube and averaged to give a single reading, since tubes sometimes do not stain evenly. An accuracy of ±0·5 mm. should be possible.

The results of analysing various gas mixtures with the palladosulphite analyser and with an infra-red analyser are compared in table I. The results of simultaneous tests using the palladosulphite analyser and an infra-red analyser are shown in table II. In 10 cases in which per-cent. extraction was measured in duplicate the maximum difference between

TABLE II—RESULTS OF SIMULTANEOUS ESTIMATIONS OF CARBON-MONOXIDE PER-CENT. EXTRACTION BY MEANS OF PALLADOSULPHITE ANALYSER AND INFRA-RED ANALYSER

—	Infra-red analyser	Palladosulphite analyser	Difference
Normals:			
1	54%	60%	+6%
2	61%	62%	+1%
3	54%	51%	−3%
4	61%	65%	+4%
5	61%	60%	+1%
Patients:			
1	28·5%	33%	+4·5%
2	42%	38%	−4%
3	25%	26%	+1%
4	36%	33%	−3%

the two readings was 10%, and the average difference 5·6%. Apparently it should be possible to obtain an overall accuracy of ±10%.

Results

Results in healthy persons and in patients with emphysema and pulmonary fibrosis are shown in fig. 2. This shows that the test discriminates reasonably well between normal and abnormal, and that in patients those with the greater incapacity have lower per-cent. extraction values.

Our values for the 14 healthy subjects ranged from 43% to 65% with an average of 52%, which are the same as found by other workers (Bates 1952, MacNamara et al. 1959).

The average per-cent. carbon-monoxide extraction in the 13 cases of diffuse pulmonary fibrosis was 34·5%, compared with 31·9% found in a similar group by MacNamara et al. (1959).

In the 9 cases of emphysema the patients were all disabled by their condition, and carbon-monoxide diffusion was considerably reduced.

Discussion

The results of diffusion measurements are usually expressed in physiological " absolute " values of millilitres per minute per millimetre of mercury—that is, as diffusing capacity—but MacNamara et al. (1959) have shown that expression of the results as per-cent. extraction of carbon monoxide discriminates no less effectively between normal and abnormal diffusion.

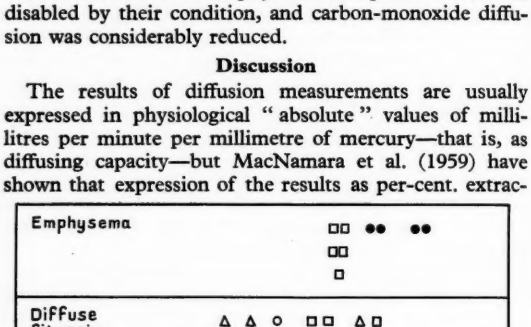

Fig. 2—Spot diagram showing distribution of values for percentage extraction of carbon monoxide in normals and in patients with diffuse pulmonary fibrosis and with emphysema.

By attempting to estimate only the carbon-monoxide per-cent. extraction we avoid many of the difficulties involved in standard methods, such as end-tidal-air sampling or arterial puncture. Also, the per-cent. extraction of carbon monoxide is unaffected by fairly wide variations in ventilation and tidal volume (Gilson and Hugh-Jones 1955, MacNamara et al. 1959); and therefore these need not be measured.

I am deeply indebted to Dr. W. M. Macleod for his help in the preparation of this paper; to Dr. J. G. Scadding, director of the Institute of Diseases of the Chest, where this method was compared with the standard diffusion test, and to Dr. F. J. Prime for his help and encouragement; to the Wessex Regional Hospital Board for facilities; to Mr. D. L. Williams, of the Southern Gas Board, for the loan of the analyser; and to my colleagues who acted as normal controls.

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". . . Thus an increase in the rate of change places an increasing strain on the machinery of democracy. This, I believe, is why democracy has broken down—or has not been attempted—in many countries where rapid industrialisation is taking place and why it is at risk everywhere. For when disturbance so overloads the adaptability of a system as to threaten its existence, the system is prone to take whatever steps seem likely to preserve its coherence. In the conflict between the urgent and the important, even freedom may seem a luxury."—Sir GEOFFREY VICKERS, *The Undirected Society*; p. 117. University of Toronto Press, 1960.

Preliminary Communications

INCREASED CUTANEOUS RESPONSE TO DILUTED AUTOLOGOUS SERUM IN HEREDITARY ANGIO-ŒDEMA

HEREDITARY angio-œdema—a rare, highly fatal disease of unknown ætiology—is inherited as a mendelian dominant trait. Clinically it is characterised by frequently recurring attacks of acute circumscribed non-inflammatory œdema involving primarily the skin, subcutaneous tissue, larynx, and gastrointestinal mucosa.[1 2] We report here the results of an investigation of the peculiar permeability-inducing properties of the serum [3 4] of a 32-year-old Caucasian woman affected with this disease since the age of 2.

The patient had a normal cutaneous response to 0·1 ml. intradermal injections of 1/10,000 histamine, acetylcholine, and 5-hydroxytryptamine. During episodes of angio-œdema, as well as during œdema-free periods, total blood histamine, the levels of 5-hydroxytryptamine, and acetylcholine esterase in the serum were normal, 24-hour blood-clots were not visibly lysed, and 24-hour urinary 5-hydroxy-3-indolacetic excretion was normal. Thus the level and metabolism of these endogenous substances, known to affect capillary permeability, were found to be normal as far as they were tested. When, however, attention was directed to the permeability-increasing factor(s) in diluted autologous serum [3 4] a significant difference in the patient's reaction to her own diluted serum was noted.

The techniques used consisted in intravenous injection of Evans blue dye (T1824), 0·5 mg. per kg. body-weight, followed in 5 minutes by the intradermal injection of 0·1 ml. of undiluted human serum or serum diluted from 1/12·5 to 1/800 in physiological saline solution.[5] Serum dilutions were allowed to stand at room temperature for 30 minutes before the intradermal injection. If the injection of treated serum caused an increase of vascular permeability, a localised area of bluing resulted. The intensity and area of the bluing at the intradermal injection site measured 30 minutes after injection was used as an index of the vascular-permeability-increasing potency of the injected material.

Neither the patient nor the eleven normal subjects, six of whom were female, showed a significant bluing response to the injection of their own undiluted (autologous) serum. The patient, however, showed a response to the injection of her own serum diluted 1/12·5 to 1/800 which was significantly greater both in area and in intensity of bluing than was elicited in any of the eleven normal subjects to the injection of their own diluted serum. For example, at a dilution of 1/25 the average bluing diameter in the patient was 15·7 mm. with a range of 14–17·1 mm., while the mean diameter of the eleven normals was 11·3 mm. with a range of 10–12·5.

From three further experiments involving the patient and five normal controls, four of whom were female, it became apparent, however, that this increased reactivity was found only when the patient's own diluted serum was injected into the patient; neither the patient's diluted serum injected into normal individuals nor the diluted sera from the normal controls injected into the patient gave an increased response. A portion of the results of one of these three experiments is shown in the table. The invariable finding that the patient's own diluted serum reacted more strongly in her than did the sera of normal individuals is seen in the table, although the difference here is not as great as in other experiments. But the main point of the table is that the patient showed no increased reactivity to the control sera, nor did her serum react in the control subjects more strongly than the sera from normal individuals. Here again, this was the invariable finding in the experiments not shown.

CUTANEOUS RESPONSE OF PATIENT AND THREE CONTROL SUBJECTS TO INTRADERMAL INJECTION OF 0·1 ML. OF AUTOLOGOUS AND HOMOLOGOUS SERUM DILUTED 1/100 FOLLOWING INTRAVENOUS EVANS BLUE 0·5 MG. PER KG. BODY-WEIGHT

Recipient	Donor	Bluing response	
		Diameter (mm.)	Intensity
Patient	Patient	14·2	2+ *
	A	9·9	1+ †
	B	11·0	1+
	C	12·0	1+
Control A	A	8·8	± ‡
	Patient	9·3	1+
	B	10·5	1+
	C	9·0	1+
Control B	B	11·1	±
	Patient	10·2	1+
	A	11·7	1+
	C	11·4	±
Control C	C	10·6	1+
	Patient	12·2	1+
	A	12·4	1+
	B	8·8	1+

* Deep blue. † Light blue. ‡ Faint blue.

The patient's two sons who have the disease were also studied, but less extensively. Both showed a significantly greater cutaneous bluing response to their own serum than did the eleven control subjects and both had a greater response to their own serum than to the diluted serum of a normal male control.

The nature of the agent in diluted serum responsible for the bluing was also investigated.

The response of the patient and normal control to injections of their own sera was completely inhibited by diluting their sera in crystalline soybean trypsin inhibitor 0·1 mg. per ml. before intradermal injection, or on the addition of the soybean trypsin inhibitor after the diluted serum had stood for 30 minutes.[3] The bluing response to diluted autologous serum was partially inhibited by diluting the serum in *e*-aminocaproic acid 0·25 mg. per ml. before intradermal injection. No inhibition occurred if autologous serum was diluted in physiological saline, allowed to stand at room temperature for 30 minutes and then diluted in *e*-aminocaproic acid to a final concentration of 0·5 mg. per ml.

There was no inhibition if the serum was diluted in the anti-histamine mepyramine maleate, 0·1 mg. per ml., or in neostigmine. Diphenylhydramine hydrochloride ('Benadryl') 0·1 mg. per ml. inhibited the patient's response to dilutions of her own serum greater than 1/200, but did not inhibit a control's response. The patient's response to diluted autologous serum was depressed while under treatment with promethazine 200 mg. by mouth daily and this depressed response correlated with clinical improvement.[6]

From these experimental data, we postulate that the disordered vascular permeability in hereditary angio-œdema is an inherited hyperresponsiveness of the skin and other tissues to an autologous serum factor which, upon activation in vivo by an unknown stimulus, increases the permeability of capillaries.

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ISOLATION OF COXSACKIE A7 VIRUS IN SCOTLAND

DURING investigations of poliomyelitis-like illness in Scotland in 1959, 37 agents were isolated by intraperitoneal inoculation of day-old suckling mice with stool extracts from which no virus had been isolated in monkey-kidney tissue cultures. The inoculated animals became paralysed, and in 35 cases histological examination showed myositis characteristic of Coxsackie group-A virus infection. The other 2 agents caused fat necrosis characteristic of Coxsackie group-B virus, and one of these was successfully adapted to tissue culture and identified as a strain of Coxsackie B5 virus. Two Coxsackie A viruses had been isolated by similar methods in 1956. Of the 37 presumed group-A Coxsackie viruses, 33 have been identified as type A7 strains.

For identification purposes, adult mice were immunised by intraperitoneal injections of 20% suspensions of carcasses of suckling mice infected with Dalldorf's prototype A7 and A14 Coxsackie viruses and with the local group-A strain 1034 isolated in 1959 from a paralysed child. Immunised mice were injected intraperitoneally with mouse sarcoma 180 and the resultant ascitic fluid was used as antiserum for the tests. A cockerel was also immunised by intramuscular injection of fluorocarbon-purified 1034 virus suspension emulsified in incomplete Freund's adjuvant ('Difco'). These sera were used for neutralisation, complement-fixation, and hæmagglutination-inhibition tests with 20% suckling-mouse-carcass suspensions as antigens.

The results of tests to identify strain 1034 are summarised in the table.

Neutralisation tests were carried out by inoculation of suckling mice, except for those against the Russian AB IV strain of Coxsackie A7 virus which were performed in monkey-kidney tissue cultures using the adapted strain of Habel and Loomis.[1] Complement-fixation tests utilised 20% suckling-mouse-carcass extracts as antigen. Prototype A7 virus and 33 isolated strains were found to agglutinate fowl red cells; this reaction could be specifically inhibited by homotypic antisera, and hæmagglutination-inhibition was used as a third serological test. The table shows that strain 1034 reacted as a type-A7 strain related both to Dalldorf's prototype and to the AB IV strain; slight neutralisation of Coxsackie A14 virus was shown by the hyperimmune-fowl antiserum to strain 1034. Normal fowl serum and ascitic fluid from non-immune mice gave no reaction in the tests.

SEROLOGICAL IDENTIFICATION OF STRAIN 1034

Antisera	Tests and virus strains								
	Neutralisation test				Complement-fixation			Hæmagglutination inhibition	
	AB IV	A7	A14	1034	A7	A14	1034	A7	1034
1034 (fowl) ..	+	+	±	+	NT	NT	NT	+	+
1034 (mouse) ..	+	+	0	+	+	0	+	+	+
A7 (mouse) ..	+	+	0	+	+	0	+	+	+
A14 (mouse) ..	0	0	+	0	0	+	0	0	0

+ = positive reaction. ± = slight neutralisation.
0 = negative reaction. NT = not tested.

Studies of the remaining strains of virus are not yet complete. One of the group-A strains failed to propagate in serial passage and was thus not available for identification studies. The fowl-cell hæmagglutination caused by the other 32 group-A strains was specifically inhibited by immune-fowl serum against strain 1034 and by immune ascitic fluid against prototype Coxsackie A7 virus. Of these 32 extracts, 27 fixed complement sufficiently strongly and specifically with Coxsackie A7 ascitic fluid to warrant classification as type-A7 strains on this basis; the other 5 strains showed weaker reactions and will be retested when stronger antigens have been prepared from them.

Neutralisation tests in suckling mice have confirmed the type-A7 character of 16 strains identified by hæmagglutination-inhibition, including the 5 whose extracts did not fix complement sufficiently strongly to warrant classification on this basis. The 3 group-A strains which produced no hæmagglutinin also failed to fix complement with type-A7 and type-A14 antisera and were not neutralised by 1034 fowl antiserum. Thus the 39 viruses isolated in suckling mice comprise 33 Coxsackie A7 strains, 4 unidentified group-A strains, 1 Coxsackie B5 virus, and 1 unidentified group-B strain.

The hæmagglutinating activity of 20% carcass extracts of suckling mice infected with the prototype and isolated Coxsackie A7 viruses was demonstrable with vaccinia-agglutinable fowl cells. Human, mouse, and vaccinia-inagglutinable fowl cells were not agglutinated. Titres of 1/16 to 1/64 were shown by various preparations tested at room temperature. Titres were about 3-fold higher at 37°C than at 4°C, and the hæmagglutination pattern remained stable for 24 hours at either temperature. Preliminary attempts to use the hæmagglutination-inhibition test to measure antibody in human sera failed because of the presence therein of nonspecific inhibitor. Nonspecific inhibition was also observed with fowl sera and mouse ascitic fluids but to low titres which did not interfere with the test for antibody. Specific inhibition titres were not changed by absorbing immune-fowl serum with mouse red cells, nor by absorbing ascitic fluids with fowl cells. Higher specific inhibition titres were obtained if serum and virus were allowed to interact for one hour before addition of the fowl cell suspension. Hæmagglutinins were not detected in 20% suspensions of carcasses of normal or Coxsackie A14 virus infected suckling mice.

Work is in progress to complete the serological tests and identify all the isolated viruses, to investigate their other properties, and to study further the hæmagglutination by Coxsackie A7 viruses.

It is also hoped to investigate the pathogenicity of these locally isolated strains: none has yet been adapted to tissue cultures of monkey kidney, HeLa, human amnion, or human thyroid, but strain 1034 caused fatal paralytic disease after intramuscular injection in adult merions. Adult mice were insusceptible to injections of this virus by intracerebral, intramuscular, or intraperitoneal routes.

Since one of the strains was isolated from a child with paralysis in 1956 (Grist et al., to be published) antibody studies are planned in order to throw light on the prevalence of infection during the past few years. A team of clinical, epidemiological, and virological workers will describe the 1959 outbreak and the illnesses of the patients from whom these viruses were isolated. That Coxsackie A7 viruses are capable of producing serious disease in man is shown by the fact that of the 33 patients from whom these viruses were isolated, 7 suffered from paralytic illnesses and 1 of these died. It may be noted that the Russian "type 4 poliovirus", isolated from 3 paralysed children in Karaganda, Kazakhstan[2] was later identified as Coxsackie A7 virus,[1 3] and that this same virus was also isolated from a paralysed child in the U.S.A.[4]

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virus. I am grateful to Dr. Gamble for recommending the use of sarcoma 180 to produce immune ascitic fluids. I am indebted to Dr. G. B. S. Roberts for histological examinations of suckling mice, and to Miss R. McLelland, F.A.T.A., and Mr. C. McLean, F.I.M.L.T., and Mr. J. Kerr for technical assistance.

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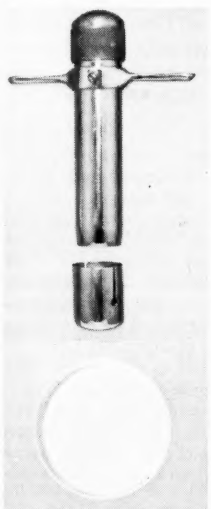
New Inventions

A COLOSTOMY TREPHINE

Sames,[1] in his description of extraperitoneal colostomy, mentions the use of a gunsmith's wad punch for cutting the hole in the skin, subcutaneous fat, and external oblique aponeurosis. For the past eighteen months I have used an instrument that consists essentially of a piece of stainless-steel tubing, 1 in. in diameter, honed to a fine edge at one end. The other end has a handle and a rounded cap which fits into the palm of the hand. The cap is detachable to facilitate cleaning; and a second cap protects the cutting edge, which is otherwise very easily damaged. A disc of 'Perspex' is used to provide counter-pressure from within the abdomen (see figure).



The trephine, which is long enough to cope with the occasional very obese abdominal wall, is held like a corkscrew and twisted right and left until the required depth is reached.

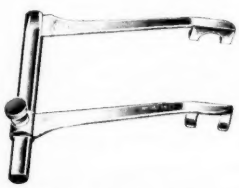
I wish to thank the department of medical physics, Royal Marsden Hospital, for making the prototypes, and the department of medical photography, Royal Marsden Hospital, for the photograph. The instrument in its present form is made for me by A. & L. Hawkins and Co. Ltd., 15, New Cavendish Street, London, W.1.

GORDON S. RAMSAY
M.B. Lond., F.R.C.S.

London, W.1

A SELF-RETAINING PALMAR RETRACTOR

MANY operations on the hand and wrist require a wide exposure through a small incision. This self-retaining retractor for the palm has been designed to facilitate single-handed surgery. It is most useful in operations for trigger finger and de Quervain's disease, in "cutting down" for intravenous cannulation, and in pædiatric surgery.



Advantages over the usual type of small self-retaining retractor lie in the provision of a slide and screw mechanism rather than a ratchet, which permits delicate adjustment of the tension of the wound margins, and in the parallel arrangement of the rake blades which ensures even retraction.

The instrument (illustrated half size) is sturdy and easy to handle. The angled arms allow it to fit snugly against the contours of the patient's hand or arm. Cleaning and sterilisation present no problem.

I am grateful to the staff of the instrument workshop at the Middlesex Hospital who made the prototype. The retractor is now available from Messrs. Down Bros. and Mayer & Phelps Ltd.

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1. Sames, C. P. *Lancet*, 1958, i, 567.

Reviews of Books

Treatment of Cancer in Clinical Practice

Editors: PETER B. KUNKLER, M.D., M.R.C.P., F.F.R., radiotherapist, United Birmingham Hospitals; ANTHONY J. H. RAINS, M.S., F.R.C.S., professor of surgery, Charing Cross Hospital Medical School. Edinburgh: E. & S. Livingstone. 1959. Pp. 821. 100*s*.

THIS book is primarily intended for those preparing for post-graduate examinations, and for them it will undoubtedly be valuable. For others it will provide a useful source of information on subjects beyond their special field. It does not set out to be a series of comprehensive monographs on all aspects of cancer treatment. The lists of references have wisely been kept short: and the text is in consequence more pleasurable to read. There is a good index.

The basic principles and techniques of surgery, radiotherapy, and chemotherapy are described in the first seven chapters. The remainder of the book deals with cancers topographically. There is a valuable chapter on the presentation of results, with admirable advice on the extraction of information from case-notes, follow-up, and the calculation of morbidity and mortality rates. If surgeons and radiotherapists always followed these simple instructions, the literature on cancer treatment would become more rational. The standards of acceptable cancer statistics laid down in this clear, short essay are maintained in most of the sections on individual cancer sites. This is largely due to frequent use of statistics from the United Birmingham Hospitals, which are based on excellent follow-up and are meaningfully presented. Not all the chapters come up to this standard in the presentation of results, however good they may be in describing the treatment. It is unfortunate that the chapters on the reticuloses and the blood contain hardly any information at all about survival-rates of treated or untreated cases. The almost complete absence of any adequately controlled, prospective studies of therapy is not the fault of the writers; few such investigations have been done. This makes it hard and often impossible to judge the relative values of different forms of treatment. The book is well illustrated and excellently produced. The cost is high but not excessive for the quality of the text and the production.

Diseases of the Chest including the Heart

Editor: J. ARTHUR MYERS, PH.D., M.D., professor of internal medicine and public health, University of Minnesota. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960. Pp. 1015. 276*s*.

THIRTY-FOUR authorities contribute to this book, which is divided into two parts, dealing with diseases of the chest and diseases of the cardiovascular system. Some of the contributions are of the highest standard—among them chapters on the segmental anatomy of the lungs, pulmonary mycoses, and chest injury, and a succinct and practical account of the assessment of pulmonary function. But others are uncritical and sometimes out of date. It is stated, for example, that there is no evidence that vaccination with B.C.G. confers dependable immunity, and that there is abundant evidence that its use has retarded tuberculosis eradication programmes. Artificial pneumothorax is still advocated as a good method of treatment for pulmonary tuberculosis, although it is admitted that its use in advanced cases has declined in recent years; and it is said to be too early to determine the true value of resection. In antituberculous chemotherapy 1 g. of streptomycin every three days is advised, although there is convincing evidence that daily administration is necessary to avoid the emergence of drug-resistant organisms. The role of *Hæmophilus influenzæ* in exacerbations of chronic bronchitis is not discussed, and it is disconcerting to find inhalations of 5–10% CO_2 and 90–95% oxygen recommended for liquefying sputum in this condition. Abdominal supports and pneumoperitoneum are still considered useful expedients in the management of emphysema. Guidance on the management of simple lung abscess is curiously vague: the section on treatment advises that a surgeon be called in as

soon as the disease is diagnosed, and an authority is quoted as recommending (in 1941) the immediate institution of external drainage; but in the section on prognosis a more recent authority is quoted as stating that surgery is increasingly less needed, and that resection has replaced drainage when it is.

The mustiness noticeable in some parts of the section on diseases of the chest is nowhere apparent in the chapters on cardiovascular disease: recent advances are in fact, featured prominently. There is a detailed and valuable discussion of the diagnosis of congenital cardiac malformations in infants and young children, and a useful and well-illustrated account of developments in cardiac surgery. Among some first-class contributions on other topics, the chapter on radiology of the heart is outstanding. As the respiratory and cardiac sections are in no way interdependent, there seems no advantage in publishing them in one rather unwieldy volume.

Much of this book is excellent, but it will fall short of the highest standard until the approach to some of the subjects is more up to date and, above all, more critical; at present it cannot be unreservedlv recommended.

Textbook of British Surgery

Vol. IV. Editors: SIR HENRY SOUTTAR, D.M., F.R.C.S., consulting surgeon, The London Hospital; J. C. GOLIGHER, CH.M., F.R.C.S., professor of surgery, University of Leeds. London: Heinemann Medical Books. 1959. Pp. 699. 105*s*.

THIS is the final volume of a series whose preceding parts have been warmly welcomed. It contains some twenty articles on such topics as wounds, burns, fractures, and bone and joint diseases, and could well have been subtitled A Comprehensive Textbook in Practical Orthopædic Surgery. The names of the seventeen contributors are sufficient warranty of its status. While most similar encyclopædias contain a chapter on fractures, the subject is commonly dealt with in a highly compressed style which is, at the best, indigestible and, at the worst, positively misleading, so Mr. John Clark is to be particularly congratulated for the way he has here discharged a difficult commission in only 70 pages. The emphasis throughout is on the practical aspects.

Biographical Memoirs of Fellows of the Royal Society 1959

Vol. 5. London: The Royal Society. 1959. Pp. 280. 30*s*.

THE latest addition to this splendid series contains, among 19 biographical studies, only 1 of a medical man, Robert Muir. Others have had medical connections; W. R. G. Atkins was for a time a captain in the R.A.M.C. and in 1942 did much routine physiological testing at medical centres throughout the country, resulting in papers on the vitamin-C reserves of troops and kindred matters. G. M. Bennett in his early years was senior demonstrator in the department of chemistry at Guy's. K. S. Lashley, an American psychologist, wrote an important monograph on *Brain mechanisms and intelligence: a quantitative study of injuries of the brain.* " It was a beautifully economical summing up of his experimental work of the preceding nine years. It quickly achieved wide recognition, and whatever may eventually prove to be the finally correct story in detail of the nervous mechanisms and their functions involved in intelligent behaviour, it is certain that Lashley's work and his exposition in this monograph will remain of fundamental importance."

Sir Roy Cameron's 25-page biography of Robert Muir is splendidly done and is enriched with recollections by some of Muir's friends and assistants. His scientific work fell into four clear-cut groups which are discussed in detail. His earliest work faced the problem of where and in what manner the blood-cells were formed and how upsets in their development brought about disease. This interest led to studies in immunity and later to the problem of hæmolysis. His last work centred round the malignant cell.

Each biography is preceded by a good portrait, and though some are illustrated with chemical formulæ and formidable equations, there are many light personal touches. For example: " As golfers, he (Muir) and I were of different species, he a tiger in his day and I a rabbit. It wasn't until I joined his staff at the mature age of 30 I learned from him that proficiency in golf was essential to progress in pathology! In the 1920s and early 30s, he used to go to Newcastle, Co. Down, with three other friendly tigers for a fortnight at Easter to play two rounds a day in all weathers—their aim in every round being to return a best-ball score of less than the average of their ages, i.e., about 68 or less." Muir's biography alone makes this modestly priced volume essential for any medical library with a good reference section.

At Your Best for Birth (and Afterwards)

EILEEN MONTGOMERY, M.C.S.P. Bristol: John Wright. 1959. Pp. 59. 5*s* 6*d*.

THE author has set down the exercises which she recommends during pregnancy, labour, and the puerperium. Great emphasis is placed upon relaxation as a means of avoiding tension, but Mrs. Montgomery is very careful not to make any unjustifiable claims for relaxation exercises, and in her summing-up she acknowledges that, even without such training as she describes, childbirth can be quite a natural and pleasing experience. The text is illustrated by excellent silhouette drawings. The section on posture and on how to lift heavy objects is particularly good and the related drawings very helpful. The patient is given sound advice on the correct shoes and clothes to wear during pregnancy. A brief account is given of the anatomy, physiology, and management of labour. The medical reader will be surprised to see a diagram likening the female pelvis to the flue of a chimney and to read that uterine action in labour is similar to that of the fingers squeezing a tube of toothpaste so that the contents are expelled. These analogies are seldom very successful.

In a small book the author has managed to include much that will contribute to the wellbeing of the pregnant woman. The primigravida, in particular, will find useful information, common-sense, and good advice.

Biochemical Values in Clinical Medicine

The Results Following Pathological or Physiological Change. ROBERT DUNCAN EASTHAM, M.D., D.C.P., consultant pathologist to the Frenchay/Cossham group of hospitals, Bristol. Bristol: John Wright. 1960. Pp. 148. 15*s*.

THIS paper-backed pocket book provides a summary of the ways in which various conditions affect biochemical tests. The investigations are arranged alphabetically for easy reference. As far as possible the principle is explained, the normal range and physiological variation of the results given, and then follow the changes in disease. The tests are not restricted to those normally performed by many routine laboratories. Some are even given with the comment that they are not useful in clinical practice—for example, the estimation of blood and urine sulphate. It is doubtful whether every reader will agree with all these comments. There are a fair number of misprints amongst the references; and in the definitions the equivalent and mille-equivalent weights of calcium are wrongly given. This excellent compendium will be widely used, particularly on the ward.

Virus Virulence and Pathogenicity (*Ciba Foundation Study Group no. 4.* London: J. & A. Churchill. 1960. Pp. 114. 12*s*. 6*d*.).—A small group of virologists met in London to discuss a series of papers on virus virulence and pathogenicity with especial reference to influenza. This book, edited by Dr. G. E. W. Wolstenholme and Miss Cecilia M. O'Connor, contains the papers and verbatim discussions, and makes instructive and stimulating reading. Although at the outset Stuart-Harris notes that it is practically impossible to measure virulence, this does not deter subsequent speakers. Anyone interested in such topics as the reason for the differing mortality in the influenza pandemics of 1918 and 1957 or the use of living attenuated vaccines, will enjoy reading the lively discussions of this distinguished group.

THE LANCET
LONDON 14 MAY 1960

Live Poliovirus Vaccine

INTEREST in attenuated poliovirus vaccines remains intense. This is because killed vaccine, though it is highly effective,[1] has certain deficiencies. It is not 100% effective; frequent booster doses may be necessary; it is not proving easy to persuade enough people to receive the injections; and the vaccine is expensive. The case for living attenuated vaccine, which has been authoritatively expressed by PAUL,[2] is based on the belief that it will overcome these deficiencies. It is thought that, since orally administered attenuated virus will imitate natural infection by the natural route, almost lifelong and complete immunity will follow one dose of each type of poliovirus, and that the living virus will confer a local alimentary resistance to reinfection that is not conferred by killed vaccine. It seems likely that resistance to the acceptance of vaccination will be overcome by an oral vaccine. Attenuated vaccine should also prove cheaper to prepare and administer. But these theoretical advantages have still to be proved in practice.

A great deal more information about living vaccine has been published—notably in the full report of the First International Conference on Live Poliovirus Vaccines,[3] held in Washington last June. Although attenuated vaccine has now been given to many millions of people without any recorded ill effects, neither its safety nor its effectiveness has been proved. The doubts about safety concern not the vaccine strains themselves (though the conditions of manufacture and testing are necessarily severe in order to ensure the genetic stability of the vaccine strain and the exclusion of contaminating microorganisms) but rather the strains excreted by those vaccinated. Excreted virus can spread to others—and indeed this capacity to spread has been used as an argument for attenuated vaccine since in this way people unwilling to be vaccinated may be protected. It is now clear that the polioviruses excreted by the vaccinated sometimes differ from the virus fed. They may show an increase in monkey neurovirulence, in ability to grow at high temperatures (40°C), or in ability to grow in low concentrations of sodium bicarbonate[4]; and they may possibly show minor changes in antigenic structure.[5] There is no evidence that virus with a greater neurovirulence for monkeys has a selective advantage in the human intestinal tract; nor is there evidence that harm has resulted from such changes. Neurovirulence for the monkey displayed after direct inoculation into the central nervous system may bear little relation to virulence for man infected by mouth, where neurovirulence will manifest itself only if the virus is invasive enough to reach the central nervous system. Nonetheless, the virus being mutable, it could possibly yield a mutant capable of causing epidemic disease in man; and this is presumably how virulent strains arise in Nature from less virulent wild strains.

The uncontrolled spread of attenuated vaccine virus in man could be limited to some extent by administering the vaccine to newborn babies. This would have other advantages. The emergence of epidemics of poliomyelitis is probably due to postponement of poliovirus infection, because of better hygiene, till later in childhood when the antibodies acquired from the mother have declined and an increased biological sensitivity to poliovirus has been acquired. Thus probably more than 99% of children would be benefited by infection with any wild type of poliovirus, let alone an attenuated one, in the first year or two of life. It has been calculated [6] in Sweden that under the age of 5 years about 3 type-1 poliovirus infections in 1000 are paralytic, whereas over the age of 25 the risk of paralysis is 20–100 times greater. The mortality also rises sharply with age—a point that should reinforce the present campaign to vaccinate people aged 26–40. Even during severe epidemics the incidence of paralysis in children has been found to be only 1–2 for every 100 infections. Thus, the younger children are when they are vaccinated the less danger there is. Other host factors besides age affect the outcome of poliovirus infection; and in mass campaigns there must always be some possibility, however remote, of causing a paralytic infection in someone of particularly great susceptibility due to physiological or genetic causes. But in view of the impressive record of safety, mainly in Russia, with the attenuated vaccines, these dangers are probably exceedingly remote and hypothetical. The difficulties in the assessment of the safety of living vaccine are clearly brought out in a study carried out in Leopoldville in the Belgian Congo.[7–9] Here the CHAT strain of attenuated type-1 poliovirus was administered in a mass campaign to children under 5 years starting in August, 1958. Shortly thereafter a severe epidemic due to type-1 poliovirus occurred in the city. The authors concluded that the vaccine was safe and about 60% effective in preventing paralysis—although, unfortunately, the vaccination campaign did not prevent the development of an epidemic. The vaccine was thought to be safe because the first cases appeared in unvaccinated patients who had had no known contact with vaccinated children. Also the genetic and serological characters of CHAT virus and virus excreted by some who did not become ill differed from the characters of viruses isolated from cases. Unfortunately, all the observed differences in characters have also been observed in attenuated polioviruses after passage in the human intestinal canal.[4 5] The balance of evidence suggests that the epidemic strain was a naturally occurring poliovirus, but the possibility that

1. See *Lancet*, Jan. 9, 1960, p. 97.
2. Paul, J. R. *Yale J. Biol. Med.* 1960, **32**, 241.
3. Live Poliovirus Vaccines: papers presented and discussions held at the First International Conference on Live Poliovirus Vaccines, Washington, D.C., June 22–26, 1959. Pan American Sanitary Bureau, Regional Office of W.H.O., Washington. $5.
4. Melnick, J. L., Benyesh-Melnick, M., Brennan, J. C. *J. Amer. med. Ass.* 1959, **171**, 1165.
5. Gard, S. *Bull. Wld Hlth Org.* 1960, **22**, 235.
6. Olin, G. Cited by S. Gard *in* Live Poliovirus Vaccines; p. 228.
7. Lebrun, A., Cerf, J., Gelfand, H. M., Courtois, G., Plotkin, S. A., Koprowski, H. *Bull. Wld Hlth Org.* 1960, **22**, 203.
8. Plotkin, S. A., Lebrun, A., Koprowski, H. *ibid.* p. 215.
9. Koprowski, H., Norton, T. W., Wecker, E., Gard, S. *ibid.* p. 243.

it was derived by mutation from the attenuated virus cannot be excluded beyond all doubt because of the lack of a really stable genetic marker. As Prof. WILSON SMITH [10] said in a discussion of virus virulence and pathogenicity:

> ". . . it seems to me that the decision when to use an attenuated strain of any virus for vaccination can never be satisfactorily justified on the most rigorous scientific grounds. It must be a decision based on other considerations, that is by an assessment of the probable risk against the probable risk of not using it."

More is known about the efficacy of killed than of attenuated vaccine. Killed vaccine is about 80–90% effective in preventing paralysis—and almost certainly more effective if only laboratory-proved cases of paralytic poliomyelitis are considered. Thus in the poliomyelitis epidemic in Detroit in 1958 BROWN et al.[11] isolated poliovirus from 77% of 241 unvaccinated cases of paralytic poliomyelitis and from 29% of 41 cases in which three doses of killed vaccine had been administered. Similarly, LENNETTE et al.[12] isolated poliovirus from 81% of unvaccinated cases of paralytic poliomyelitis in children under 5 years and from 36% of cases in which two or more doses of vaccine had been given; in this study, 2% of unvaccinated and 21% of vaccinated patients harboured an enterovirus other than poliovirus. This evidence suggests that some cases of paralysis are due not to poliovirus but to other viruses. The proportion of cases of paralysis that cannot be shown to be due to poliovirus increases with additional doses of vaccine. There is some evidence that paralysis not due to poliovirus is milder and more transient. It was found by BROWN et al.,[11] for example, that residual paralysis occurred in 84% of confirmed poliovirus cases with paralysis in the acute stage and in 60% of those who failed to yield poliovirus. KOKKO and MURRAY [13] in the U.S.A. have found that unselected commercial killed vaccine gives a conversion-rate of 89% for type 1 following three doses of vaccine in children aged 6 months to 3 years. For the most part the efficacy of killed vaccine has been assessed relatively soon after three doses. The efficacy of living vaccine in preventing paralytic poliomyelitis has not yet been assessed in a statistically controlled trial of the type applied to killed vaccine. The difficulties of such a trial when the virus can spread to the unvaccinated are immense. In some trials reliance has been placed on the incidence or mortality of paralytic poliomyelitis, but this can be most misleading. In Sweden,[14] for example, the number of cases of poliomyelitis has steadily declined from that in the peak epidemic year of 1953; but this is not due to the introduction of killed vaccine, which was not used on a large scale until 1957: it is due rather to natural fluctuation in incidence. In assessing the effectiveness of attenuated vaccine, therefore, serological tests have to be relied on. In general the responses have been good, especially in converting individuals without antibodies to relatively high levels—higher as a rule than are obtained from a primary course of killed vaccine. There is, however, one important reservation, illustrated particularly clearly in the study by PLOTKIN et al.[8] at Leopoldville. Here of individuals who previously lacked type-1 antibodies only 60% developed them after being fed this type (CHAT strain). This disappointing result was almost certainly due to interference by other enteroviruses which are known to circulate freely in the area.[15]

At the Washington meeting BODIAN [16] pointed to the need for independent assessment of the claims of the various candidate attenuated polioviruses developed by COX, KOPROWSKI, and SABIN. Further investigation is still required on several important points: the antigenic effectiveness at different ages and following different doses, using the viruses either singly or in combination; the persistence of the antibody response; and the stability of the genetic characters of the virus excreted by those vaccinated. In view of the proved effectiveness of killed vaccine, this is still the method of choice for preventing poliomyelitis; and in order to achieve the best results its acceptance should be promoted by an energetic vaccination programme. There is, however, a clear need to improve the method of prevention—by means either of attenuated vaccine or of more potent killed vaccine perhaps combined with diphtheria, tetanus, and whooping-cough prophylactics.

Medicine and Apartheid

As doctors we cannot be unconcerned by the effects of the South African policy of racial segregation on the quality of medical care. Medically, *Apartheid* has two inimical effects: it splinters the profession into discrete groups according to race; and it prevents the free application of skill.

When the Government's new provisions are given effect, the medical schools of Witwatersrand and Cape Town must join those of Pretoria and Stellenbosch in refusing admission to non-whites, just as Durban is obliged to discriminate against whites. Despite opposition by the profession, the Durban school is apparently to come under the provisions of the Separate Universities Act, whereby the Minister of Education will control its policy and appoint and discipline its staff. The staff of the non-white colleges may be dismissed by him if they " comment adversely upon the administration of any department of the Government ", or if they " impede, obstruct or undermine the activities of any Government department ".

Inevitably the quality of training will be lower in the medical schools for non-whites. A main factor sustaining standards in most civilised countries is the free exchange—of people as well as of knowledge—between one university and another; but in South Africa such exchange will be restricted. The universities for non-whites will further suffer by being administered vir-

10. Smith, W. *in* Virus Virulence and Pathogenicity; p. 104. Ciba Foundation Study Group no. 4; London, 1960.
11. Brown, G. C., Lenz, W. R., Agate, G. H. *J. Amer. med. Ass.* 1960, **172**, 807.
12. Lennette, E. H., Magoffin, R. L., Schmidt, N. J., Hollister, A. C., Jr. *ibid.* 1959, **171**, 1456.
13. Kokko, U. P., Murray, R. *Bull. Wld Hlth Org.* 1960, **22**, 263.
14. Gard, S., Böttoger, M., Lagercrantz, R. *in* Live Poliovirus Vaccines, p. 350.
15. Vandeputte, M. *Bull. Wld Hlth Org.* 1960, **22**, 313.
16. Bodian, D. *in* Live Poliovirus Vaccines; p. 683.

tually as departments of the Government—a form of administration which has been rightly shunned elsewhere in the world. The establishment of separate registers for doctors of different racial groups has been foreshadowed in at least one Ministerial statement (such registers have already been set up for nurses under the all-white South African Nursing Council); and provincial administrations have imposed a descending scale of remuneration for white, Indian and Coloured, and African doctors. Such differentiation will seem unacceptable to most doctors: while remuneration can properly be decided according to competence or even seniority, it should not be determined by colour. Nor is the profession hampered only by these restrictions. Clinical practice is impeded by, for instance, the separation of white from non-white patients in hospitals, by the distinction of white from non-white nurses, and by the Government's ban on non-white persons giving transfusions of blood to the white.

We have repeatedly drawn attention to this interference with medicine.[1] A group of British doctors who have written to us, prompted by the state of affairs in South Africa, where twelve doctors have lately been arrested,[2] propose concerted action to aid our colleagues in that country. Their call will evoke widespread sympathy; but, as these twelve doctors are being detained without trial, we cannot be sure of the grounds for their arrest. If the arrests were made in an effort to interrupt the free practice of medicine, as a profession we should unitedly protest. If, on the other hand, they resulted from political actions or opinions, then, while those who wish may protest as citizens, such arrests do not concern us as a profession. This distinction is not always easy; for politics impinge on every aspect of all our lives, and under an illiberal regime doctors may be forced to commit themselves politically in order to protect their patients: the temporary arrest of the medical superintendent of Baragwanath Hospital, Johannesburg, after the Sharpeville shooting may be an example. Nevertheless we should seek to preserve the distinction; for if as a professional group we are to be heeded we should seek to exert influence only when we can do so from our special insight. Even with this limitation, there is fully enough to occupy us.

1. *Lancet*, 1957, i, 675, 746, 891, 941, 978, 1096, 1182; *ibid.* 1957, ii, 702.

2. Joffe, M. *Brit. med. J.* April 23, 1960, p. 1279

Annotations

PSYCHIATRY AND THE PÆDIATRICIANS

APPRECIATION of mental factors in disease is slowly spreading in the non-psychiatric specialties, but nowhere has the psychological approach made more strides than among pædiatricians. Dr. Thomas Stapleton's farewell address at St. Mary's Hospital Medical School on April 25 was notable because few " organic " doctors are so fully aware that, for example, it is often a matter of chance whether a child is referred to psychiatrist, juvenile court, or pædiatrician. He pointed to the manifold ways in which emotional factors of one kind or another seem to determine physical disorder, and to those in which abnormality is passed down the generations. Psychoanalytic observations have given clues to understanding these disorders, and the knowledge gained must be spread more widely—such dissemination being preferable, he believed, to an enormous increase in the number of psychiatrists. These observations also help towards prevention. Thus we now know something of the need to avoid separation of mother and child if at all possible, and to adjust adoption procedure so that no child is deceived. Contrasting the Russian approach with our own, however, he mentioned that two experts from the U.S.S.R. said last year in Montreal that children placed in residential nurseries from two months old develop better and more quickly than those in families, and rarely become delinquent.

Dr. Stapleton has doubts about our arrangements for problem families, where " a small army " of people have access to the house; and he feels that material aid may even be an inducement to some households to sink low enough to receive it. The training of family doctors is, he thinks, especially critical if only so that the practitioner shall refer patients to the right specialist; for otherwise they will return with the wrong answers. But above all he put the need for research: fact must be distinguished from fancy, and he hopes, in his chair of pædiatrics in Sydney, to start a prospective study to elucidate the origins of homosexuality, prostitution, and delinquency. Though longitudinal surveys have been made (e.g., that of Douglas and Blomfield [1]), the data are not yet adequate for psychiatric purposes. The most useful figures we have on delinquency and crime start rather late in life, at an average of about 11 years old,[2] and Dr. Stapleton is right in his research priority. But a longitudinal study large enough to tell us about the three factors which interest him may give us much (or more) of value on the background of neurosis and psychosis. Careful evaluation of early family environment is very difficult, and Dr. Stapleton deserves good wishes both on his new appointment and on this onerous undertaking.

CHRONIC RENAL FAILURE

WHEN a patient has died from chronic renal failure, the kidneys show a great variety of lesions of the glomeruli, tubules, blood-vessels, and interstitial tissues; and the abnormalities in the different functions observed during life might be assumed to be related to lesions of the corresponding parts of the surviving nephrons. In the Lumleian lectures of 1952, however, Platt [3] showed that, though chronic renal failure has many causes, the commonest being chronic glomerulonephritis, chronic pyelonephritis, and essential hypertension, all of which have a common structural basis of a diminished number of functioning nephrons, the functioning remnant is hypertrophied (hence the enlarged glomeruli and dilated tubules with apparently flattened epithelium) and working at an increased rate; and furthermore the symptoms and signs of renal failure are due to pushing of the physiological adaptation of the reduced number of persisting nephrons beyond normal limits: most if not all of the functional dis-

1. Douglas, J. W. B., Bloomfield, J. M. Children under Five. London, 1958.
2. McCord, W., McCord, J. Origins of Crime. New York, 1959.
3. Platt, R. *Brit. med. J.* 1952, i, 1313, 1372.

turbances are those which in animal experiments result from reducing the number of surviving nephrons. This is most easily understood in connection with substances excreted predominantly by glomerular filtration, such as urea and creatinine: a decrease in the number of nephrons must result in retention in the body-fluids, if the rate of acquisition remains constant: as the plasma levels rise, the filtered load per residual nephron increases until a new equilibrium is reached. For most other functions it is difficult to define the capacities of nephrons in diseased kidneys, since, once a patient has Bright's disease, data can no longer be compared with control observations on the same subject, the chemical changes already present may affect the function of various parts, and finally there may be partly damaged nephrons with either glomerulus or tubules acting normally and the other part disordered, thus upsetting the whole basis of functional controls.

Bricker et al.[4] have now reviewed their experiments in which these difficulties have been overcome. In dogs in which two separate urinary bladders had been formed they induced unilateral chronic chemical nephritis, chronic pyelonephritis, and chronic glomerulonephritis and in each series compared the function of the diseased kidney with the normal on the other side under various test conditions while the internal environment was kept essentially normal. The various series all showed an absolute decrease in values for all renal functions in the experimental kidney. But the functional capacity of the remaining nephrons was unimpaired: thus the ratio of the glomerular filtration fraction to the effective renal plasma-flow, the maximum rate of secretion of *p*-aminohippurate, and the maximum rate of glucose reabsorption were all the same, in the three types of diseased kidneys, as in the normal controls—suggesting that no anomalous nephrons were present. Similarly, studies on the concentrating and diluting mechanisms of the diseased kidneys showed that these remained virtually intact; but the fewer the remaining nephrons the more advanced were the adaptive changes, the chief adaptation being a greater rate of solute excretion per nephron leading to relative isosthenuria. The patterns of excretion for sodium, chloride, and potassium were all similar in the diseased kidney to those in the normal, with remarkable ability to maintain normal plasma concentrations. From comparison of these findings with the series of events in chronic renal failure, Bricker et al. concluded that the diseased kidneys have a gradually diminishing number of nephrons, but that these retain normal functional capacity, that the functional changes relate to adaptive changes imposed by the decreased number of nephrons and resultant changes in body-fluids, that the flexibility of function decreases as the number of nephrons decreases, and that this occurs in an orderly and predictable pattern.

In a comprehensive review of pyelonephritis, Kleeman et al.[5] point out that, while the pathological changes in the chronic pyelonephritic kidney are complex and pleomorphic, the functional patterns for the remaining nephrons are more or less normal: the most reasonable explanation is that the majority of renal glomeruli and tubules, severely altered by the disease processes, are non-functioning while the tests measure the relatively normal function of the residual units and show no glomerulotubular imbalance.

Thus chronic renal failure should not be regarded as a haphazard series of disordered functions resulting from haphazard lesions of different parts of nephrons; and, as Platt[3] recommended, the aim in treatment should be to reduce the work of the kidney by restricting protein intake but giving liberal amounts of salt and of water, for the last of which the patient's instinctive demands are usually the most accurate guide.

4. Bricker, N. S., Morrin, P. A. F., Kime, S. W. *Amer. J. Med.* 1960, **28**, 77.
5. Kleeman, C. R., Hewitt, W. L., Guze, L. B. *Medicine, Baltimore*, 1960, **39**, 3.

CEREBELLAR CORTICAL DEGENERATION IN ALCOHOLICS

NEARLY a hundred years ago Samuel Wilks[6] noted that heavy drinkers of brandy, or of "the diabolical compound called absinthe" across the Channel, were liable to become paraplegic although sometimes the symptoms were "almost confined to the legs, resembling in character, those of locomotor ataxia". He believed that in these patients the volatile oils dissolved in the alcohol had given additional force to its poisonous effects.

That there is a form of chronic cerebellar degeneration to which alcoholics are liable has been recognised in recent times only since Romano et al.[7] described 5 cases in 1940. Other reports have followed, and no less than 16 cases were reported by Chodoff et al.[8] Victor et al.[9] have now described the pathological findings in 11 instances, 4 of them symptomless, which came to necropsy. The atrophy, which sometimes is obvious to the naked eye, is almost confined to the vermis and especially the anterior and superior parts (including the lingula, central lobule, and culmen) and so is liable to be missed unless the cerebellum is cut in the midsagittal plane. All cellular layers are involved, especially the Purkinje cells; for this and other reasons Victor et al. regard this as a zonal, and not just a transynaptic, degeneration. Cell loss in the olives was noted in all but 2 of these cases, and occasionally the dentate nucleus showed a loss of cells. They have found 11 reported cases in alcoholics with cerebellar changes comparable to those they describe.

Victor et al. studied 46 cases clinically. In half of them the onset was rapid (in 1 case it dated from an episode when the patient was trying to avoid road traffic); in 16 it was slow; and in 7 the disorder was mild for a time and then became rapidly worse. Although, in general, progression was associated with continued drinking and poor nutrition, exacerbations seemed to be related to neither: in some the disorder actually worsened during a period of abstention, and occasionally accentuation of the symptoms dated from an accident or an operation. Thus Victor et al. find it difficult to believe that the toxic action of alcohol is the primary cause of the degeneration, but of their patients three-quarters were malnourished when they first came under observation. The ataxia involved especially the legs and gait, which is in keeping with the pathological findings and the known somatotopic representation of limbs in the vermis. In a few cases, however, there was incoordination of the arms and thickness of speech. Occasional findings were nystagmus, ocular dysmetria, and rhythmical tremor with certain sustained postures. Half the patients had an associated polyneuritis, the presence of which may mask slight cerebellar impairment. Half of them had clinical evidence of liver disease, and in 14 cirrhosis was present. 4 had Wernicke's encephalopathy, and a few had signs of hepatic encephalo-

6. Wilks, S. *Med. Times Gaz.* 1868, **2**, 470.
7. Romano, J., Michael, M., Merritt, H. H. *Arch. Neurol. Psychiat.* 1940, **44**, 1230.
8. Chodoff, P., Auth, T., Torepin, H. *J. nerv. ment. Dis.* 1956, **123**, 376.
9. Victor, M., Adams, R. D., Mancall, E. L. *Arch. Neurol.* 1959, **1**, 579.

pathy. Two-thirds of these patients complained of their "rubber legs" before the age of 50; the youngest patient was 31.

Victor et al. place occlusion of the vertebral and basilar arteries high on the list for differential diagnosis, with multiple sclerosis as an alternative not to be forgotten—and even Wilson's disease, because rhythmical tremor when present tended to be in proximal groups of muscles. Most difficulty was found in distinguishing this condition from resolving Wernicke's encephalopathy: they point out, however, that in the latter the ataxia is limited to the function of stance and gait and is not manifest during individual movements of the legs.

The neuropathologist will be interested in the variety of Purkinje-cell changes noted in the seemingly healthy controls; and the classifier of disease will view with interest, and perhaps criticise, the attempt of Victor et al. to dispose of all known forms of cerebellar cortical degeneration in six categories.

HÆMOGLOBIN MOLECULE

ONE of the triumphs of modern chemistry has been the analysis of the aminoacid sequence in insulin, for which Frederick Sanger received a Nobel prize in 1958. The hæmoglobin molecule has also attracted special attention because of its physiological importance. Aminoacid sequences have been determined, and Ingram [1] discovered that the difference between normal and sickle-cell hæmoglobin was due to the difference in one single aminoacid in one of its constituent chains. Ingram's work is a development of the protein analysis pioneered by Sanger.

The hæmoglobin molecule, which, like other proteins, consists of polypeptide chains, is remarkable for having four ferroporphyrin groups which are thought to be attached to these polypeptide chains by histidine side-chains. In human hæmoglobin the chains have been identified by their terminal aminoacids which, in adult hæmoglobin, are valyl-leucyl in one (the α-chain) and valyl-histidyl-leucyl in the other (the β-chain). In human fœtal hæmoglobin the α-chain of adult hæmoglobin is combined with a third type of chain—the γ-chain—which has glycyl as its terminal aminoacid residue. Each molecule consists of four chains—two α and two β chains in adult hæmoglobin, and two α and two γ chains in fœtal hæmoglobin.[2] A change in the aminoacid sequence of either the α or the β chains results in abnormal hæmoglobins.[3] No variant of the γ chain has yet been reported. Two abnormal hæmoglobins have been described as having no α chains. Hæmoglobins H and Barts are composed only of β and γ chains respectively.[4 5]

The hæmoglobin molecule is not a long fibre but a spheroid, and the polypeptide chains must, therefore, be bent in many places to fit into this shape. It is here that the physicists take over to determine the shape of the polypeptide chains and thence the microstructure of the hæmoglobin molecule. Indeed, if aminoacid sequence determines the way in which these polypeptide chains are bent, it might one day be possible to conclude that a certain aminoacid sequence must be present because a polypeptide chain was found to be of a given shape. Vice versa, one might be able to determine the bending and cornering of a polypeptide chain in a protein molecule simply by determining the aminoacid sequence.

Our knowledge of the physical structure of the hæmoglobin molecule is based on work done on horse hæmoglobin by Dr. Max Perutz and his colleagues in Cambridge, and on the research carried out on the related simpler chromoprotein, myoglobin, which his colleague Dr. J. C. Kendrew has been pursuing, using material obtained from the whale. Two important communications on the three-dimensional structure of these protein molecules have been published by these workers and their collaborators from the Medical Research Council unit for molecular biology at the Cavendish Laboratory in Cambridge and the Davy-Faraday research laboratory, Royal Institution, London.[6 7] Kendrew and Perutz have also addressed the Royal Institution, where they were introduced by Sir Lawrence Bragg, who is associated with the first use of X rays to determine crystal structure. His object at the time was rock salt, and it must have given him satisfaction to see his technique now applied to much more complicated molecules.

Unlike hæmoglobin, myoglobin does not consist of four polypeptide chains but of one only. It contains 153 aminoacids and only one hæm. It is an intracellular pigment which serves for the temporary storage of oxygen. The form of the myoglobin molecule is spheroidal. Many polypeptide chains of protein are not straight chains but are arranged in the shape of a spiral, the helix, according to a brilliant hypothesis first put forward by Pauling and Corey,[8] which has now been confirmed. The α-helix arrangement, however, would still not explain the spherical form of the myoglobin molecule, and the additional bending of the spiral "staircase" has been examined by shining X rays through myoglobin crystals.

The use of the X-ray-reflection technique for measuring distances between atoms in protein molecules has been made practicable by Perutz's observation that the combination of heavy atoms with such molecules produces changes in the position of reflections seen in the X-ray photograph. By adding two heavy atoms, points of reference are made which allow a quantitative interpretation of the distances between the reflections. According to the distance between the X-ray reflections, different structures can be determined. By using $1^1/_2$ Å one obtains about 20,000 reflections per myoglobin molecule, which indicates that individual atoms are being photographed. With 2 Å, giving 10,000 reflections, it is possible to picture the configuration of the individual chains, and with 6 Å (400 reflections) it is possible to photograph the convolutions of the chain in the myoglobin molecule, because the distance between flexures is about 6 Å. Thus, $1^1/_2$ Å reveals the primary structure, 2 Å the secondary, and 6 Å the tertiary structure of the myoglobin molecule.

The tertiary structure was discovered by Kendrew some years ago, when he demonstrated a peculiar worm-like model which portrayed the convolutions of the main chain in the myoglobin molecule. Though the aminoacid sequence of myoglobin was quite different in the sperm-whale and the seal, the tertiary structure seemed to be very much the same in both. Dr. Kendrew [7] has now reported on the completion of stage II, in which the arrangement of the main chain and the position of side-chains were photographed. This was no mean effort, and

1. Ingram, V. M. *Nature, Lond.* 1956, **178**, 792; *ibid.* 1957, **180**, 326.
2. Schroeder, W. A. *Prog. Chem. org. nat. Prod.* 1959, **17**, 322.
3. Ingram, V. M. *Brit. med. Bull.* 1959, **15**, 27.
4. Jones, R. T., Schroeder, W. A., Balog, J. E., Vinograd, J. H. *J. Amer. chem. Soc.* 1959, **81**, 3161.
5. Hunt, J. A., Lehmann, H. *Nature, Lond.* 1959, **184**, 872.
6. Perutz, M. F., Rossmann, M. G., Cullis, A. F., Muirhead, H., Will, G., North, A. C. T. *Nature, Lond.* 1960, **185**, 416.
7. Kendrew, J. C., Dickerson, R. E., Strandberg, B. E., Hart, R. G., Davies, D. R., Phillips, D. C., Shore, V. C. *ibid.* p. 422.
8. Pauling, L., Corey, R. B. *Proc. U.S. nat. Acad. Sci.* 1951, **37**, 235.

the interpretation of the 10,000 reflections required something like 250,000 computations. The main chain turned out to have a hole in the middle and to have a helical structure of exactly the type predicted by Pauling and Corey. The helices are right-handed; and of the 153 aminoacids 70% are arranged in that way, the remainder presumably forming the side-chains. Eight lengths of α-helix could be differentiated, and the iron atom was seen to be attached to the main chain through a histidine side-chain. The X-ray photographs were made on crystals, and on the side of the iron opposite to where it was attached to the histidine side-chain water could be seen. This water is thought to take in crystals the place which in vivo is occupied by oxygen.

In the case of hæmoglobin Perutz and his team determined, first of all, where the hæm groups are placed. They are arranged in two pairs, 34 and 36 Å apart. By using an aperture of $5^1/_2$ Å four polypeptide chains could be identified; and there were two types of chains, each of which was present in duplicate. One of the two chains resembled the myoglobin chain more than the other. The two identical hæmoglobin chains seemed to be closely linked, and the amino-group end of one was very near to the carbonyl end of the other within the molecule.

It is still not easy to understand why once one hæm has become oxygenated, the second hæm is oxygenated twice as fast, and the third three, and the fourth twenty times, faster. The hæm groups are not close to each other; but, as Dr. Perutz pointed out at the Royal Institution, the various hæms may possibly be linked by sulphydryl groups which facilitate the passage of oxygen.

POLIOMYELITIS-LIKE ILLNESS

THE recovery of Coxsackie viruses, particularly those of the B group, from patients with aseptic meningitis, or "non-paralytic poliomyelitis", has often been reported; and the recovery of these viruses from the cerebrospinal fluid, taken in conjunction with the epidemiological evidence, leaves little doubt of the ætiological role of these viruses. Less commonly, Coxsackie viruses of group A have been shown to have an ætiological role in aseptic meningitis. But the association of Coxsackie viruses with an illness which closely resembles paralytic poliomyelitis is sufficiently unusual to merit comment.

In 1952 Chumakov et al.[1] in Russia observed three children with what was thought to be bulbospinal poliomyelitis, from whom they isolated a virus which they could not identify. In monkeys the virus caused paralysis, with poliomyelitis-like lesions on histopathological examination of the central nervous system. But the virus was antigenically distinct from poliovirus types 1, 2, and 3; and Chumakov et al. understandably called it type-4 poliovirus. The Russian workers did not have access to Coxsackie typing sera, but workers in the U.S.A. and in Sweden were able to show that the Russian virus was in fact a Coxsackie virus A type 7. Coxsackie A7 viruses have been found to cause aseptic meningitis in the past, but reports of paralytic disease have been rare. One such instance was described by Ranzenhofer et al.[2] in the U.S.A. in 1958, and this week we publish on p. 1054 a preliminary account by Dr. Grist of further isolations of Coxsackie viruses from cases of poliomyelitis-like illnesses in Scotland. Of 33 patients from whom Coxsackie A7 viruses were isolated 7 had paralytic illnesses, and 1 of these died. The clinical and epidemiological findings will be awaited with interest. Possibly paralytic infections with Coxsackie A7 virus in people vaccinated with poliomyelitis vaccine may sometimes give a false impression that the vaccine has been inefficacious.

1. Chumakov, M. P., Voroshilova, M. K., Zhevandrova, V. I., Mironova, L. L., Itzelis, F. I., Robinson, I. A. *Probl. Virol.* 1956, **1**, 16.
2. Ransenhofer, E. R., Dizon, F. C., Lipton, M. M., Steigman, A. J. *New Engl. J. Med.* 1958, **259**, 182.

W.H.O.

THE World Health Organisation has faults as well as virtues, and some of them are reflected in the annual report of the Director General.[1] The medical reader, at least, would prefer a shorter survey containing more numerical data. Nevertheless its list of current projects (which makes up about half the book) is a very inspiring catalogue of genuine endeavours to make this a healthier and happier world.

Malaria can be abolished, and there is hardly a country where eradication is not in progress or at any rate planned. The doctors have done their part, and the responsibility for paying the bill lies with the politicians. There will be more mouths to feed, but many millions more with the energy to raise their standards of living. Given the will and the money, smallpox and yaws could likewise be completely suppressed; and in all these measures W.H.O. has shown the way. News of the great plagues no longer depends upon the arrival of a ship with the yellow jack in the rigging: patient clerks in Geneva sort weekly returns from all over the world to warn port officers of what may be on the way. Few countries cursed with trachoma have the resources for constructive research. Thanks to W.H.O., laboratories in many lands collaborate on this problem—and with some success. The report lists about 500 projects on these and many other subjects. Europe, as is proper, gets less attention than those parts of the world where a man is old at 40. Almost every country receives local help in one or more fields, and all enjoy their share of travelling fellowships lasting from one month to two years.

Of all the benefits of W.H.O. these last are of outstanding value—and not only to the recipients. London (and every other great centre of learning) at this moment houses men and women from all over the globe who spend their days in clinics and laboratories learning by sharing in the day-to-day work—and there is no better way. A streptococcus offers much the same problems in London or Sarajevo or Casablanca (which in the eyes of W.H.O. is in Europe). And it would warm any Londoner's heart to hear from quondam fellows in some far-off place how kindly they feel about institutions in Keppel Street or the Whitechapel Road. They are the wandering scholars of today, who treasure their experiences when the big men on the committees have to refer to their diaries to remember where they were three months ago. All this work of W.H.O. is done by a staff of less than 2000 (to whom, by the way, the United Kingdom contributes the largest contingent) on a meagre income of about $16 million. The rich countries subscribe more heavily, and we hope they always will.

1. The Work of W.H.O., 1959: Official Records of the World Health Organisation no. 98. Obtainable from H.M. Stationery Office, P.O. box 569, London, S.E.1. Pp. 283. 10s.

THE next session of the General Medical Council will open on Tuesday, May 24, at 2.15 P.M., when Sir DAVID CAMPBELL, the president, will deliver an address. The Disciplinary Committee will sit on Wednesday, May 25, at 10.30 A.M.

Special Articles

A PROPOSED STANDARD SYSTEM OF NOMENCLATURE OF HUMAN MITOTIC CHROMOSOMES

The following statement has been drawn up by a study group, which met to formulate an agreed system of nomenclature for human chromosomes, with a view to eliminating the confusion which has arisen from the independent publication of a variety of systems by different workers.

THE rapid growth of knowledge of human chromosomes in several laboratories, following advances in technical methods, has given rise to several systems by which the chromosomes are named. This has led to confusion in the literature and so to the need for resolving the differences. Consequently, at the suggestion of Dr. C. E. Ford, a small study group was convened to attempt the formulation of a common system of nomenclature.

The meeting was arranged, through the good offices of Dr. T. T. Puck, to be held at Denver, in the University of Colorado, under the auspices of the Medical School. The meeting of this study group was made possible by the support of the American Cancer Society, to whom grateful thanks are due. For practical reasons, it was decided to keep the group as small as possible and to limit it to those human cytologists who had already published karyotypes.* In addition, three counsellors were invited to join the group to guide and aid the discussions and, if necessary, to arbitrate. Fortunately, the last office did not prove necessary, and it was possible by mutual agreement to arrive at a common system which has flexibility.

It was agreed that the principles to be observed by the system should be simplicity and freedom, as far as possible, from ambiguity and risks of confusion, especially with other systems of nomenclature in human genetics. It should also be capable of adjustment and expansion to meet the needs of new knowledge of human chromosomes. The system should be agreed to by the greatest possible proportion of cytologists working in the field, but the risk that a minority may be unable to accept the system as a whole should not be allowed to delay adoption by a majority.

It was agreed that the autosomes should be serially numbered 1 to 22 as nearly as possible in descending order of length, consistent with operational conveniences of identification by other criteria. The sex chromosomes should continue to be referred to as X and Y, rather than by a number which would be an additional and ultimately a superfluous appellation.

It was generally agreed that the 22 autosomes can be classified into seven groups, distinction between which can readily be made. Within these groups further identification of individual chromosomes can in many cases be made relatively easily. Within some groups, especially the group of chromosomes numbered 6–12, including also the X chromosome, the distinctions between the chromosomes are very difficult to make by presently available criteria. However, lesser difficulties are encountered in separating chromosomes 6 and the X from the remainder of this group. It is believed that, with very favourable preparations distinction can be made between most, if not all, chromosomes.

It is proposed that the autosomes first be ordered by placing the seven groups as nearly as possible in descending order of size. Within each group the chromosomes are arranged, for the most part, by size. It was desired specifically to avoid the implication that the size relationships have been permanently decided in every instance, but it is hoped that the assignment of numbers will be permanently fixed. In those cases where distinction is at present doubtful, final definition of each chromosome can be left until further knowledge has accrued, though an attempt is made to provide a characterisation of each. These principles make it possible to draw up a conspectus of the chromosomes, a table of their quantitative characteristics and a table of the synonyms which authors have already published. These are appended (tables I, II, and III).

In table II, showing the diagnostic characters of the chromosomes, three parameters are relied upon. These are:

(1) The length of each chromosome relative to the total length of a normal X-containing haploid set—i.e., the sum of the lengths of the 22 autosomes and of the X chromosome, expressed per thousand.

(2) The arm ratio of the chromosomes expressed as the length of the longer arm relative to the shorter one.

(3) The centromeric index expressed as the ratio of the length of the shorter arm to the whole length of the chromosome.

The two latter indices are, of course, related algebraically quite simply, but it is thought useful to present both here. In some chromosomes, the additional criterion of the presence of a satellite is available (table I), but in view of the apparent morphological variation of satellites, they and their connecting strands are excluded in computing the indices.

Table II shows the range of measurements determined by various workers. Some of the variation expresses the uncertainty due to measurement of relatively small objects; but many of the discrepancies between different workers' observations are due to the measurement of chromosomes at different stages of mitosis and to the effect of different methods of pretreatment and preparation for microscopic study. The ranges shown, therefore,

TABLE I—CONSPECTUS OF HUMAN MITOTIC CHROMOSOMES

Group 1–3	Large chromosomes with approximately median centromeres. The three chromosomes are readily distinguished from each other by size and centromere position.
Group 4–5	Large chromosomes with submedian centromeres. The two chromosomes are difficult to distinguish, but chromosome 4 is slightly longer.
Group 6–12	Medium-sized chromosomes with submedian centromeres. The X chromosome resembles the longer chromosomes in this group, especially chromosome 6, from which it is difficult to distinguish. This large group is the one which presents major difficulty in identification of individual chromosomes.
Group 13–15	Medium-sized chromosomes with nearly terminal centromeres (" acrocentric " chromosomes). Chromosome 13 has prominent satellites on the short arms. Chromosome 14 has small satellites on the short arms. No satellites have been detected on chromosome 15.
Group 16–18	Rather short chromosomes with approximately median (in chromosome 16) or submedian centromeres.
Group 19–20	Short chromosomes with approximately median centromeres.
Group 21–22	Very short, acrocentric chromosomes. Chromosome 21 has satellites on its short arms. The Y chromosome is similar to these chromosomes.

* In contemporary publications the terms, karyotype and idiogram, have often been used indiscriminately. We would recommend that the term, *karyotype*, should be applied to a systematised array of the chromosomes of a single cell prepared either by drawing or by photography, with the extension in meaning that the chromosomes of a single cell can typify the chromosomes of an individual or even a species. The term, *idiogram*, would then be reserved for the diagrammatic representation of a karyotype, which may be based on measurements of the chromosomes in several or many cells.

TABLE II—QUANTITATIVE CHARACTERISTICS OF THE HUMAN MITOTIC CHROMOSOMES

All measurements were made from cells of normal individuals, except those made by Fraccaro and Lindsten, which included cases of Turner's syndrome. Column A is the relative length of each chromosome, B is the arm ratio, and C the centromere index, as defined in the text.

—	Tjio and Puck [6]			Chu and Giles [2]			Levan and Hsu [5]			Fraccaro and Lindsten *			Lejeune and Turpin [4] *			Buckton, Jacobs, and Harnden *			Range		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
1	90	1·1	48	90	1·1	48	85	1·1	49	82	1·1	48	87	1·1	48	83	1·1	48	82–90	1·1	48–49
2	82	1·6	39	83	1·5	40	79	1·6	38	77	1·5	40	84	1·5	40	79	1·6	38	77–84	1·5–1·6	38–40
3	70	1·2	45	72	1·2	46	69	1·2	45	65	1·2	45	67	1·2	46	63	1·2	46	63–72	1·2	45–46
4	64	2·9	26	63	2·9	26	63	2·7	27	62	2·6	28	62	2·6	25	60	2·6	28	60–64	2·6–2·9	25–28
5	58	3·2	24	58	3·2	24	59	2·6	28	60	2·4	29	57	2·4	30	57	2·4	30	57–60	2·4–3·2	24–30
X	59	1·9	34	57	2·8	38	52	1·6	38	54	1·6	38	58	2·2	32	51	1·7	37	51–59	1·6–2·8	32–38
6	55	1·7	37	56	1·8	36	56	1·7	37	54	1·6	38	56	1·7	37	56	1·6	38	54–56	1·6–1·8	36–38
7	47	1·3	43	52	1·9	35	51	1·9	35	50	1·7	37	51	1·8	36	50	1·7	37	47–52	1·3–1·9	35–43
8	44	1·5	29	46	1·7	29	48	1·6	33	47	1·7	37	48	2·4	29	46	1·5	40	44–48	1·5–2·4	29–40
9	44	1·9	40	46	2·4	38	47	1·8	36	45	2·0	33	47	1·9	35	44	2·1	32	44–47	1·8–2·4	32–40
10	43	2·4	27	45	2·3	30	45	2·0	33	45	2·6	34	45	2·6	27	44	1·9	35	43–45	1·9–2·6	27–35
11	43	2·8	34	44	2·1	32	44	2·2	31	43	2·2	31	44	1·6	39	43	1·5	40	43–44	1·5–2·8	31–40
12	42	3·1	24	43	3·1	24	42	1·7	32	43	1·7	37	42	2·8	27	42	2·1	32	42–43	1·7–3·1	24–37
13	35	8·0	11	32	9·7	10	32	5·0	16	34	4·8	17	33	6·8	14	36	4·9	17	32–36	4·8–9·7	10–17
14	32	7·3	12	34	9·5	9	37	4·0	18	35	4·4	19	32	7·0	13	34	4·3	19	32–37	4·3–9·5	9–19
15	29	10·5	9	31	11·9	8	35	4·7	17	33	4·6	22	31	10·0	9	34	3·8	22	29–35	3·8–11·9	8–22
16	32	1·8	36	27	1·6	38	30	1·4	42	31	1·4	42	29	1·4	41	33	1·4	31	27–33	1·4–1·8	31–42
17	29	2·8	26	30	2·1	33	29	2·4	30	30	1·9	35	29	3·1	23	30	1·8	36	29–30	1·8–3·1	23–36
18	24	3·8	21	25	3·8	22	25	2·6	28	27	2·5	29	26	4·2	21	27	2·4	29	24–27	2·4–4·2	21–29
19	22	1·4	41	22	1·9	34	24	1·2	40	25	1·3	43	22	1·4	42	26	1·2	45	22–26	1·2–1·9	34–45
20	21	1·3	44	19	1·3	44	21	1·2	40	23	1·3	43	20	1·2	43	25	1·2	46	19–25	1·2–1·3	40–46
21	18	3·7	21	15	6·8	13	13	2·5	28	19	2·5	29	15	2·3	31	20	2·5	29	13–20	2·3–6·8	13–31
22	17	3·3	23	12	6·0	14	16	2·0	33	17	2·3	30	13	4·0	20	18	2·7	27	12–18	2·0–6·0	14–33
Y	19	∞	0	11	∞	0	18	4·9	17	22	2·9	26	18	∞	0	18	4·9	17	11–22	2·9–∞	0–26

* Unpublished data.

represent the maxima and minima of the means found by different workers using different techniques. However, within any one worker's observations, the variations are not so broad.

Reference should be made to two other matters of nomenclature. In the first place, it is considered that no separate nomenclature for the groups is needed. It is considered that any group to which it may be necessary to refer will be a sequence of those designated by Arabic numerals. Hence, any chromosome group may be referred to by the Arabic numerals of the extreme chromosomes of the group, joined together by a hyphen —e.g., the group of the three longest chromosomes would be Group 1–3. This scheme has the merit of great flexibility. For instance, chromosomes X and 6 may be separated from the Group 6–12 whenever they can be distinguished.

TABLE III—SYNONYMY OF CHROMOSOMES AS PUBLISHED BY VARIOUS WORKERS

New chromosome number	Tjio and Puck [6]	Chu and Giles [2]	Levan and Hsu [5]	Ford, Jacobs and Lajtha [3]	Böök, Fraccaro, and Lindsten [1]	Lejeune, Turpin, and Gautier [4]
1	1	1	1	1	1	G1
2	2	2	2	2	2	G2
3	3	3	3	3	3	G3
4	4	4	4	4	4	G4
5	5	5	5	5	5	G5
6	6	6	6	6*	6	M1
7	7	7	7	(8)	7	M2
8	8	8	8	(9)	8	Md1
9	9	9	9	(11)	9	M3
10	10	10	10	10	10	Md2
11	11	11	11	(12)	11	M4
12	12	12	12	(13)	12	Md3
13	18	14	20	14	14	T1
14	19	15	18	15	15	T2
15	20	13	19	16	13	T3
16	13	17	15	19	16	C1
17	14	16	13	17	17	P1
18	15	18	14	18	18	P2
19	16	19	16	20	19	C2
20	17	20	17	21	20	C3
21	21	21	22	22	21	Vh
22	22	22	21	23	22	Vs
X	X	X	X	?(7)	X	X
Y	Y	Y	Y	Y	Y	Y

* In the published idiogram the chromosomes of group 6–12 (including X) were indicated by discontinuous lines and left unnumbered owing to the uncertainty of discrimination at that time. For the purpose of this table, these chromosomes have been assigned the numbers shown in parentheses, in serial order of length.

1. Böök, J. A., Fraccaro, M., Lindsten, J. *Acta pædiat.* 1959, **48**, 453.
2. Chu, E. H. Y., Giles, N. H. *Amer. J. hum. Genet.* 1959, **11**, 63.
3. Ford, C. E., Jacobs, P. A., Lajtha, L. *Nature, Lond.* 1958, **181**, 1565.
4. Lejeune, J., Turpin, R., Gautier, M. *Ann. Génét.* 1959, **2**, 41.
5. Levan, A., Hsu, T. C. *Hereditas*, 1959, **45**, 665.
6. Tjio, J. H., Puck, T. T. *Proc. Nat. Acad. Sci.* 1958, **44**, 1229.

Secondly, there is the problem raised by the abnormal chromosomes which are being encountered in the more recent studies. Their nomenclature was discussed without a definite conclusion being reached. Broadly, it was agreed, however, that any symbol used should avoid incorporating a specific interpretation which was not reasonably established. It was suggested that arbitrary symbols, prefixed by a designation of the laboratory of origin, should usually be assigned to the abnormal chromosome.

In this connection, two further requisites for coordination of research were discussed. One is the storage of documentation for reference, perhaps in a central depository, additional to what it may be possible to publish. The other is the desirability that cultures be preserved, by the satisfactory methods now used, so that they are available for reference, comparison, and exchange.

Some consideration was also given to the desirability of using a uniform system for presenting karyotypes and idiograms, but recognising that individual variation in taste is involved, rigidity of design was thought undesirable. However, it was recommended that the chromosomes should be arranged in numerical order, with the sex chromosomes near to but separated from the autosomes they resemble. It is desirable that similar ones be grouped together with their centromeres aligned.

It is recognised that choice between the different possible schemes of nomenclature is arbitrary, but that uniformity for ease of reference is essential. Hence, individual preferences have been subordinated to the

common good in reaching this agreement. This human chromosomes study group therefore agrees to use this notation and recommends that any who prefer to use any other scheme should, at the same time, also refer to the Standard System here proposed.

We are well aware of the wide interest in the work of this study group and realise that this meeting is merely a preliminary to a larger meeting. It is believed that two needs have to be met in this respect. One is for seminars and workshops at which workers in the field may exchange information; such seminars are best arranged regionally. The second need, which may come later, is for international conferences; and we believe that congresses and other organisations whose interests include human genetics, should promote such meetings.

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Points of View

THE PRESS, THE PATIENT, AND THE HOSPITAL DOCTOR

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PEOPLE have always interested themselves in each other's medical and surgical adventures. The growth of popular means of communication has fostered this interest, and spread it to general hospital and health matters as well as to rare and peculiar diseases. A distinguished or notorious patient has always been " news ", and sooner or later his story will be bound to get into newspapers and on to the air. The new element is the contemporaneous detail which modern methods encourage and provide. The facts must come hour by hour from the bedside. For doctors and hospitals not to recognise and to make allowance for this is to invite difficulty and disturbance.

The medical and nursing staff require peace of mind, freedom from personal molestation, and a quiet atmosphere in which to work. It is sensible to consider in advance how best to protect them. Reporters and editors have their own point of view, which like all professional viewpoints leads to methods and to behaviour difficult for the rest of the community fully to understand. Looked at from the outside what they demand is the whole story in all its details at the earliest moment, if possible before anyone else hears it, and better still to the exclusion of anyone else. At the worst, if they cannot scoop an exclusive story it must on no account be scooped by another paper. Even with the most detailed story the reporter suspects that something important is being withheld. He has a technique for starting conversations which is almost impossible to parry; and he is adept at building a story even when his victim is uncommunicative. His knowledge of human beings has taught him the worst—gold or vanity will turn most keys.

When the Press is regarded and treated as an intruder, the reaction is fierce: the attack is launched with no holds barred, and with artifice worthy of some better purpose. This is when reporters and cameramen disguise themselves and climb the fire-escapes. Possible informers are molested in person and by telephone. Any titbit of news is elaborated; rumour and fancy are tricked out as fact; concern with accuracy dissolves. News of a kind is printed, for the public is entitled to news. Nothing else matters. The doctor and the hospital have lost their peace.

The patient or the relatives are in worse case. They cannot hide or escape, and to their natural anxieties are added the pestering of the newsmen. They can secure a limited protection. National newspapers are prepared to pay to make contracts, the main purpose of which is information, with exclusive rights as an important secondary consideration. There is probably no form of contract that will compel relatives or patients to tell everything that they know, but they can agree only to talk to the paper's accredited representative. The losing papers will accept defeat of this kind and retreat discomfited. Where any such contract has been signed, the hospital and its staff should know of it although they are certainly not bound by its terms. Some doctors are angry and refuse to treat patients who are party to such contracts. If undesirable publicity is likely to result there is justification for such an attitude. The arrangement should be discussed in a friendly spirit, when everything will depend on the patient's discretion.

Some lessons can be learned from recent experience at Saint Bartholomew's Hospital in the case of the Siamese twins. The publicity problem was simplified because of the nature of the case. Antenatal X-rays produced the diagnosis, so that there was plenty of time to make plans. The immediate nced was absolute secrecy; and by the loyalty of the hospital staff of all grades and by the common sense and discretion of the parents, the babies were delivered, remained for a month at Queen Charlotte's Maternity Hospital, and were moved to Saint Bartholomew's without comment. This gave the parents a period of peace in which to accommodate themselves to their remarkable situation. Intrusion into their privacy would have been intolerable. But once such an unusual event as this is the subject of rumour the Press is bound quite soon to find out who and where the patients are. The race to be the first on the scene is on. The lure of

scooping the news and the fear of being scooped leads inevitably to ill-mannered behaviour. The hue and cry which lasted two days should not have occurred. A factual statement should have been prepared giving the medical details for release as soon as there was the slightest suspicion of Press interest. Such a statement should be as full as possible and should include an approximate forecast of the nature and the timing of treatment. It should, of course, not be made, nor need it be signed, by any of the doctors concerned. It should come from one of the administrative officers, and it should be sent to the Press agencies, not to any one newspaper.

The agencies and individual reporters should be told that any reasonable questions will be submitted to the doctors and will be answered unless there is a good reason against this. All the staff concerned should agree not to hold any individual conversations with reporters, who do accept the idea that the hospital is giving out useful information but that it is being channelled through one hospital officer to the agencies. Reporters will fight for some exclusive detail for a while but a pattern of behaviour can be built up quickly which, if the hospital cooperates, gives the Press confidence and saves its reporters time and energy. An appetite for detail can be assuaged by serving a surfeit.

Periodic progress bulletins were sent to the agencies. The Press interest was measured by the amount of space devoted to the case and the number of telephone inquiries. The announcement of details was timed to some extent to meet demand.

The parents did not wish to know the exact day or time of the operation, nor did the hospital want an invasion by reporters. It was therefore agreed that this important piece of information should be withheld. With the exercise of some ingenuity, and again helped by the loyal silence of those directly concerned, the long operation was almost completed before the Press got wind of it. The announcement was to be made on the day after the operation, when the fate of the twins could be more clearly known. A plan had, however, been made to release a statement, should it appear that any news had reached the Press. The objects of this were to forestall a scoop and to ensure accuracy. Once more the plan partly failed. One newspaper telephoned the parents a little time before the hospital to report that the operation was complete. The official statement was immediately released. The next day a long account followed, giving many medical details, and an assessment of the prognosis and including the names of the more senior medical staff concerned. With this it would have been sensible to send appropriate photographs. Clearly the Press regarded the episode as of the greatest public interest. The surgeon became the target for camera marksmanship for some days after the operation—an aggravating state of affairs which could have been prevented had it been accepted as proper practice for photographs to be taken by the agencies or released with the news. A freely offered photograph for general distribution is less likely to be published than one secured specially and by stealth. While public interest remained acute, daily bulletins were issued. The actual Press reports were studied, and when some flight of fancy appeared about plans or details the true statement was included in the next bulletin. There were no disputes and no denials, but reporters saw that serious inaccuracies would be shown up and acted accordingly.

As time passed, interest waned and bulletins were more widely spaced. The hospital promised, and kept its promise, that any important change would be revealed to the Press agencies and that due notice would be given of the date of discharge. Surveying the course of this case the exercise of forethought and attention to detail seem to have been worth while. At no time did publicity matters get out of hand.

Some morals may be drawn and lessons learned from this experience. It is of the first importance in these days that such an unusual case should be recognised as of legitimate public interest. Preparation must therefore be made as to how the Press is to be handled. A consistent, agreed, and cooperative policy can lead to the establishment of confidence and mutual respect between all the parties concerned. Information should be available for reporters to the limit of what is seemly. Professional anonymity cannot be maintained unless the whole of the Press agrees to such a policy. Without this agreement members of the staff concerned are best safeguarded by the release of some information about what part they play, and availability of photographs would save them from being hunted.

Conference

LIVER DISEASE

A MEETING of the International Association for the Study of the Liver was held at the Royal Free Hospital, London, on April 25 and 26 under the presidency of Prof. SHEILA SHERLOCK.

Bilirubin Metabolism

Dr. I. M. ARIAS (New York) had studied bilirubin excretion in normal and clinically jaundiced (Gunn) rats. He emphasised that conjugation of bilirubin in the liver was a different process from its excretion into the bile. The Gunn rat, for instance, could excrete injected conjugated bilirubin but not the unconjugated form; here the defect was in conjugation. The normal animal could excrete both forms. In contrast, after treatment with norethandrolone (' Nilevar ') both the Gunn and the normal rat failed to excrete conjugated bilirubin, showing that norethandrolone interfered, not with conjugation, but with the excretory process.

Dr. J. CAROLI (Paris) reported extensive histochemical studies on the liver and spleen of a patient with pigmentary hyperbilirubinæmia (Dubin-Johnson-Sprinz syndrome). He believed that the black pigment in the spleen was an abnormal adrenochrome (melanin). He also noted that a secondary rise in bromsulphalein level in the serum after intravenous injection was diagnostic of this condition. Dr. S. BRANDSTAETTER (Haifa) found this disease fairly common among young male Jews of Persian origin. He had been unable to detect melanin in the spleen in two instances.

Prof. M. MASUDA (Tokyo) reported the presence of " free " bilirubin only in the serum of the fœtus and the newborn. This could easily pass the blood/brain barrier and so reach the brain. It was significant in the ætiology of neonatal jaundice.

Dr. R. WILLIAMS and Dr. B. H. BILLING (London) confirmed the fall in serum-bilirubin levels in patients with hepatitis given steroid therapy. The decrease was

steep in the first twenty-four hours, and the shape of the serum-bilirubin curve then fell exponentially. There was no change in the survival of erythrocytes after steroids, nor could the fall be accounted for by alterations in urinary or fæcal pigment excretion. Dr. W. H. J. SUMMERSKILL (Mayo Clinic) reported similar results in patients with obstruction to major bileducts, and wondered whether steroids altered the solubility of bilirubin in the tissues. Dr. ARIAS thought this unlikely. He had given steroids to one patient with jaundice due to carcinoma of the pancreas who also had multiple lipomas. Serial biopsies showed less bilirubin in the lipomas after steroid therapy.

Changes in Obstructive Jaundice

Prof. T. KITANI (Osaka) had found by electron microscopy underdevelopment or absence of microvilli lining the bile canaliculi in the human fœtus. He had also shown in obstructive jaundice in adults that there was a communication between the liver cells linking the microvilli with the sinusoids. Dr. HANS POPPER (New York) had noted disappearance of microvilli in extrahepatic biliary obstruction, "cholangiolitic" hepatitis, and drug jaundice. Norethandrolone produced stunting and irregularity of the villi, whereas chlorpromazine had no such effect. Cholestasis was independent of inflammatory changes in the portal zones. He concluded that there was no certain method of distinguishing extrahepatic from intrahepatic obstructive jaundice. Prof. G. DOMINICI and Dr. F. ORLANDI (Perugia) had noticed dilatation of the endoplasmic reticulum spaces in obstructive jaundice. They also could not distinguish histologically between extrahepatic and intrahepatic cholestasis.

Veno-occlusive Disease

Prof. K. R. HILL (London) described the world distribution of veno-occlusive disease of the hepatic venules. It was due to poisoning with monocrotaline—a member of the pyrrolizidine group of alkaloids. He had produced lesions in the hepatic venules of rats given monocrotaline, and this substance had also caused changes in tissue cultures of liver cells.

Toxic Changes

Prof. H. KALK (Kassel) reported eight cases of poisoning with trichlorphenol, an insecticide. The liver remained enlarged and the thymol-turbidity test positive, but the most remarkable change was the gross pigmentation of the liver cells, continuing in one case for four and a half years after exposure. There was no cirrhosis. Dr. T. C. CHALMERS (Boston) had noted increased pigmentation in the livers of alcoholics after the fat had disappeared. Dr. M. ROYER and Dr. B. NOIR (Buenos Aires) found that cortisone diminished ferritin fixation in the liver.

Syndrome Following Virus Hepatitis

Dr. S. J. M. GOULSTON (Sydney) described a series of young patients with malaise, nausea, and hepatic tenderness persisting after acute virus hepatitis. Hepatic biopsy showed cellular infiltration in the portal zones with no disturbance of architecture. Steroid therapy led to portal zone scars but was not always successful. The picture differed from that of active, "juvenile" "lupoid" hepatitis; for lupus-erythematosus cells were not found, endocrine changes were not seen, other organs were not involved, and serum γ-globulin was not increased. Dr. J. DE GROOTE (Louvain) had seen similar cases and believed that cure was possible even after three years' ill-health. Prof. P. N. WAHI (Agra) believed that when such a condition smouldered on for a long time the end-result was cirrhosis.

Persistent Jaundice with Cirrhosis

Dr. A. E. READ and Prof. C. V. HARRISON (London) described forty-five patients (eleven men and thirty-four women) with cirrhosis and jaundice lasting longer than three months. Forty were less than forty years old, a third gave a previous history of hepatitis, and in two-thirds the onset was insidious. The many associated conditions included nephritis, rheumatic fever, pulmonary infiltration, Hashimoto's thyroiditis, and disseminated lupus erythematosus. Serum-γ-globulin levels were very high. Microscopic examination showed an active cirrhotic lesion with cellular infiltration with plasma cells and lymphocytes. Steroid therapy resulted in increased well-being, control of associated lesions, and return of the menses. Complications of therapy included excessive weight gain and sepsis, especially of the skin. Relapse might follow cessation of steroid therapy. Patients survived for about five years after diagnosis, but ten patients in fact were alive five years afterwards.

Acute Hepatitis

Dr. R. A. KING and Dr. E. R. CULLINAN (London) had followed up cases of acute hepatitis in the Forces in the late war and had found twenty-seven instances of definite cirrhosis. Twenty-four of these were of the serum variety, and only three were preceded by acute infective hepatitis.

Treatment of Cirrhosis

Dr. PETER DYKES (Birmingham) had treated thirteen cirrhotic patients with fluid retention by intravenous salt-poor human albumin, giving 50 g. daily until the serum colloid osmotic pressure was normal. Sometimes as much as 1500 g. was needed. Three patients lost their predominant œdema, and five of ten their ascites. Those responding showed an expansion of their plasma volumes. In successful cases serum-albumin levels were maintained over long periods by infusions of albumin 50 g. every one to two weeks. Increased well-being was conspicuous, and four patients were leading active lives. Dr. PERRY J. CULVER (Boston) noted that if the serum-albumin level rose by more than 0·5 g. per 100 g. albumin infused the result was usually satisfactory.

Dr. W. V. MCDERMOTT, Jr. (Boston), had treated intractable ascites in cirrhotics by "double" portacaval anastomosis, both ends of the portal vein being joined separately to the inferior vena cava. Of seventeen patients fifteen survived the operation, and fourteen were relieved of their ascites; subsequently episodes of hepatic precoma developed in three.

Dr. C. L. GANTT (Chicago) had treated sixteen cirrhotic patients with ascites by spironolactone, an aldosterone antagonist. Seven had a diuresis, and failures often later responded when chlorothiazide was added. One patient unsuccessfully treated with spironolactone had a normal urinary aldosterone excretion, and necropsy showed a blocked portal vein. Dr. R. MORRISON and Dr. T. C. CHALMERS (Boston) had noted hyponatræmia after the

combined use of spironolactone and chlorothiazide; the addition of prednisone increased water loss and prevented this complication. Dr. S. SHALDON and Miss J. MCLAREN (London) had added mannitol as an osmotic diuretic. Of fourteen patients so treated ten lost their ascites; five of these no longer needed spironolactone, but in five ascites reaccumulated and spironolactone therapy was being continued. Dr. SUMMERSKILL believed that 1400 mg. spironolactone was sometimes needed for a few days before diuresis ensued. In four patients uræmia followed diuretic therapy with spironolactone and chlorothiazide; and this was related to loss of tonicity of body-fluids, more sodium than water being excreted.

Hepatic Blood-flow

Dr. J. CAESAR, Dr. L. GUEVARA, and Dr. L. CHIANDUSSI (London) had measured hepatic blood-flow by the extraction of ^{131}I-labelled denatured human albumin from the blood. The mean flow in healthy subjects was 1576 ml. per minute, compared with 852 ml. per minute in cirrhotics. There was evidence that part of the blood flowing through the liver in cirrhosis was not perfusing the sinusoids. Dr. A. NEUMAYR (Vienna) had measured hepatic blood-flow before and after inflation of a Senstaken œsophageal compression tube. He estimated the flow through œsophageal varices to be 300 to 500 ml. per minute.

Portacaval Anastomosis

Dr. BRANDSTAETTER believed that a rise in the glutamine content of the cerebrospinal fluid after oral ammonium chloride might indicate a tendency to neuropsychiatric complications after a portacaval anastomosis. This might be useful in the selection of patients.

Blood-pyruvate

Dr. J. M. WALSHE (Cambridge) and Dr. H. ORREGO (Santiago) reported a failure of lipoic acid to influence blood-pyruvate levels after glucose loading in cirrhotic patients. Of sixteen patients with Wilson's disease ten had abnormal pyruvate levels after glucose.

Public Health

Infectious Diseases in England and Wales

Disease	Week ended April				
	2	9	16	23	30*
Diphtheria	1	3	3	7	3
Dysentery	2465	2547	1745	1228	1199
Encephalitis:					
Infective	2	3	2	4	3
Postinfectious	2	6	1	3	4
Food-poisoning	273	229	131	130	137
Measles, excluding rubella	2466	2143	2124	2487	2273
Meningococcal infection	24	24	12	22	20
Ophthalmia neonatorum	28	25	22	23	16
Paratyphoid fever	3	3	1	..	4
Pneumonia, primary or influenzal	441	465	297	362	342
Poliomyelitis:					
Paralytic	3	2	2	4	4
Non-paralytic	2	..	2	2	1
Puerperal pyrexia	144	192	159	156	169
Scarlet fever	1054	1171	795	708	520
Smallpox	..	..	..	..	..
Tuberculosis:					
Respiratory	430	467	376	378	458
Meninges and C.N.S.	5	1	3	7	6
Other	52	38	47	50	64
Typhoid fever	1	..	..	3	2
Whooping-cough	943	916	694	815	994

*Not including late returns

Medicine and the Law

Homosexual Tendencies Not Cruelty

A WIFE petitioned for divorce on the ground of her husband's alleged cruelty. The parties had been married in 1943, when the husband was 33 and the wife 29. There were two children of the marriage. The wife's complaint was that since 1945 the husband had desired to dress up and behave like a woman.

In 1945 she had discovered women's clothing in her husband's suitcase. He had explained that by saying that in his youth he had dressed up as a woman. In 1955, when the husband thought that she was visiting her parents, she had returned to the matrimonial home to find that he had women's clothes, cosmetics, and powders in the bedroom. When challenged, he had cried and asked for her help. The wife had suffered severe shock, had a complete nervous breakdown, and from June until September, 1955, was a patient in a sanatorium, suffering from agitated depression for which she received electrical treatment. The husband refused to have treatment. In April, 1958, the wife, coming home early, found her husband in the bedroom dressed like a woman. He told her that he wanted to be a woman and live with another man. Thereafter they lived at arm's length until December, 1958, when the wife left.

Her petition was undefended, but the Special Commissioner dismissed it on the ground that cruelty had not been made out. The wife appealed, and the Court of Appeal dismissed her appeal.

Lord Justice WILLMER said that the doctor who had attended the wife in 1955 had said that she was at first suffering from agitated depression but that by October, 1955, she had sufficiently recovered to give a lucid account of what had happened.

He had been asked: " Are you prepared to say that she had been greatly affected in her health ?" and had replied: " At that time she suffered from very severe shock. She felt he was obsessive and tried to conceal from herself the full extent of his perversion. But as she realised its full extent she became more and more shattered. She was disgusted with this thing ". Another doctor who had attended her later said that a recurrence of the 1955 breakdown was a distinct possibility.

The decisive thing in the present case was the secretive nature of the husband's activities. He had done his best to conceal his tendencies and had only indulged them when he could reasonably suppose that he would not be discovered. Had he openly paraded his tendencies, knowing that they would distress his wife, cruelty would have been established. But he concealed them, and that made it impossible to impute to him any intent to injure his wife. Nor could the inference to injure her be drawn from his refusal to have treatment. The real cause of the wife's distress was not his abnormal behaviour but the fact that she had little sexual attraction for him. Treatment would not have remedied that matter. Therefore the decision of the Special Commissioner that cruelty had not been made out was right, and the wife's appeal would be dismissed. Lord Justice HARMAN and Lord Justice SELLERS delivered concurring judgments.

Bohnel *v.* Bohnel. *Court of Appeal:* Sellers, Willmer and Harman *L.J.J.* May 2, 1960. Counsel and solicitors: Roger Ormrod, Q.C., and George Dobry (Pennington & Son).

NORMAN PRIMOST
Barrister-at-Law

In England Now

A Running Commentary by Peripatetic Correspondents

WE who live in cities but cherish memories of the countryside may still be made to feel that we are a part of Nature. Now and then, a thunderstorm will burst upon our heads, or a sudden wind will topple the idols of masculine elegance and tumble the artificial edifices of haute coiffure. At such times there is a sense of clinging to the Earth with prehensile toes, of peering through the coarse fronds of unkempt hair, face to face with the old gods. In these elemental moments we are back to the wild mating of falcons and the "long, long thoughts" of youth. Paradoxically, the turbulence of natural forces then compels us to reconsider our destiny and we catch a glimpse of subjects worthy of the great essayists. It can happen in a twinkling—whenever there is an eddy in the orderly flow of Time: hiding from the rain in a doorway, a speck of dust in the eye, the pause before a sneeze. Any event can do it, so long as it is too unruly for the powers of puny Man to withstand or to control.

It was, as a matter of fact, while I waited for the electric toaster that I lit upon a short description of the new Chinese bicycle. The peculiar idiosyncrasy of this machine is that a canvas fan is mounted on the handlebars and linked by a chain to the gear system. When the cyclist is delayed by a demoniac head-wind in his hasty ride to work, the fan rotates and so assists him in his struggle with the pedals. The stronger the wind, the faster turns the fan and the faster runs the bicycle, so we are told.

Now I own with humility that the principle of this device raises physical—almost metaphysical—problems and doubts which I am unable to resolve. For example, one might argue that the thing would only work if the losses due to drag and friction were less than the torque transmitted to the wheels. If this were so, then surely it should work even in still air? One can see in the mind's eye how the rider, first pushing his conical hat more firmly down on his head and hitching up his trousers, might run a few yards with the cycle to get up speed and then leap on—with a whirr and a rattle, round spins the blue canvas propeller, faster and faster as the diabolical mechanism acts back on itself, the hitherto inconvenient back-thrust of the air now lending added impetus to the vis-a-tergo. With ever-increasing velocity and legs flying round like a centrifuge we see him at last, disappearing from view across the Paichong plains.

What if some coldblooded thermodynamician sneeringly points out a fallacy, refers slightingly perhaps to the conservation of energy, and proves that the invention has in fact only added to the immemorial burden of the coolie? It may be so; but if there is greatness in defying the thunderstorm, in being engulfed by a sneeze, then how much more greatness there must be in flouting the very Laws of Nature! What Science forbids, Poetry decrees. We should be grateful that so much of the old China still survives.

* * *

Insulated by a devoted nursing staff from my colleagues, the telephone, and the patients, I had much time to read and to reflect. Omar Khayyam was a rediscovered delight. From that I moved to the more mundane medical journals and, too introspective to read the clinical articles, thumbed over to the doings of the Royal Colleges. The names of those recently admitted as members or fellows were vaguely familiar—Khan and Mahmood; El Sherrawy and Rifkind; Budagolu and Abdul Rahman. I had met them before. There they were—there in the Rubáiyát—Jamshyd and Kaijobad; Zal and Rustum; Hatim and Mahmud:

> "Into this Universe, and *Why* not knowing
> Nor *Whence*, like Water willy-nilly flowing;
> And out of it, as Wind along the Waste,
> I know not *Whither*, willy nilly blowing."

But how did they manage in Glasgow? Had they an interpreter? The fearful garrulous harridan of a Glasgow mother, protecting her speechless infant at the pædiatric clinical, a "Vessel of a more ungainly make", explaining with a simplicity and clarity that left each candidate speechless: "Tae let understaun, Doactor, the wean's been hinging back and furrit for nigh a foartnicht. Gae toutie in fact."

* * *

There is no doubt that we are not as tough as our forebears. On the right of our house is a chicken farm run by a frail-looking old lady of 79. Her chickens and eggs are the best for miles around because the chickens run free in the orchards and are well fed. She is blind in one eye, nearly stone deaf, and has survived two major operations. She gets up at 5 A.M. and goes to bed at 9 P.M., and rules her daughter and the chickens with a rod of iron.

To gain her attention so as to order eggs or a chicken you have to toll a large bell on her back porch. She does not hear the bell but her four dogs tell her when it is rung. If she is carrying a 56 lb. sack of meal on her back she will put it down gently and then deal with your order. Once I rashly offered to carry a large bale of hay for her. Seventy yards later she took it off me without ceremony and continued the journey holding the bale on her shoulder with one hand whilst she selected the right key to the shed from a key-ring the size of a saucer which was slung round her hips on a chain. She hasn't changed at all in the ten years we have known her.

Next door on the other side is a couple who have just collected Granny to live with them. Granny is 87 and hitherto has looked after herself and has refused to be moved. But last year she started to forget things, so after a stand-up fight she was moved next door, but she cannot remain idle. At the moment she is washing down the walls (which are spotless) and she has insisted on their redecoration. She sits on the top of a ladder and when she has finished all she can reach she yells downstairs to be moved along a few feet. They were very worried in case she fell, but as she is cottage-loaf in shape her centre of gravity is very low when sitting down, and anyway she's enjoying herself and there is comparative peace. Soon the house will be completely redecorated. They are spinning it out as much as they can until the Seville oranges come in, but they have removed most of the empty jam-jars because they remember the last time she made jam and couldn't, or wouldn't, stop. After that there will be the rhubarb and then the gooseberries, but despite these plans I notice that they wear a slightly hunted look next door. Even television is a mixed blessing because now Granny has had her cataracts removed she's determined to see the programmes to the bitter end. Being old, she needs little sleep—and there are still the walls of the pantry to finish . . .

* * *

"I would have thought that in the circumstances the solution was eminently simple."

"What exactly do you mean by *I would have thought*? Do you, for example, wish to convey that you have given this problem no previous attention, but that had you done so the solution would have stuck out like an organ-stop? Or do you wish to tell me that there is no problem, that any half-wit other than myself would be able to see that the logical answer was so and so? Perhaps you are concealing something? Maybe it is the fact that you have given this problem a great deal of thought and that you have fixed ideas on its solution. Perhaps this is one of your pet tub-thumps. But being a well-mannered chap you wish to clothe your convictions with an air of educated nonchalance. Perhaps you haven't the slightest idea what it was I said. Perhaps you are unsure of yourself. I would have thought that a serious self-analysis on these lines should constitute a major contribution to your thinking."

* * *

ELMS IN APRIL

Green snow suspended in mid-air,
The new, soft leaves float around trees
Whose trunks, dressed still in thick, stained coats
Could surely not claim kin with these
Fantastic, frivolous and fair
Ethereal motes of greenery.
Yet those boles raise sap from deep roots;
Earth's distilled riches flow unseen,
Are filtered through to meet the sun.
The sunlight into life has run;
Age knows no loss of dignity
When the tall trees spin silken green.

Letters to the Editor

EXPIRED-AIR RESUSCITATION

SIR,—I was interested in the article of April 2 by Professor Woolmer and his colleagues. From the evidence presented by them, and by previous workers in this field, there seems no doubt of the efficacy of this method of resuscitation. The following incident, however, has raised a doubt in my mind.

A short time ago I was called to see a lightly built man of average height, aged 45, who had collapsed at his work. I arrived about 30 minutes after the collapse. Holger-Nielsen artificial respiration was being efficiently performed by a competent medical attendant and had been for 20 minutes. After a brief examination I considered the victim was probably dead. Nevertheless, I cleared a small amount of vomitus from the mouth, covered the lips with a handkerchief and performed mouth-to-mouth artificial respiration. Having previously seen Dr. Safar's film and used a manikin, I was as competent as anyone was likely to be. The chest rose and fell excellently, but after three or four breaths a very large quantity of vomitus was extruded from the mouth. This was again cleared and a further attempt was made. Things went quite well for a few minutes and the medical attendant then took over from me, continuing for about five minutes. During this time I made further examination and decided that beyond doubt the victim was dead. The artificial respiration was stopped. I noticed the abdomen was slightly distended and I gently pressed the epigastrium with a resultant reflux of a further pint of vomitus.

The past history of this man, as obtained from his superiors, suggested chronic renal disease and hypertension with a history of attacks of unconsciousness. He also had an enormous appetite and would eat vast quantities of food—a pound of cheese and loaf of bread at a sitting were apparently not at all unusual.

The postmortem report showed that the man was chronically anæmic, and that he had bilateral polycystic disease of the kidneys. The cause of death was acute congestive heart-failure. The stomach contained mucus only and no vomitus was present in the bronchial tree. Thus, mouth-to-mouth artificial respiration had effectively emptied the stomach.

Several questions arise:

Was this regurgitation simply due to displacement of stomach contents by air, or was it due to strong excursions of the diaphragm on an overfull flaccid stomach, or a combination of these?

Would the use of an airway have altered this situation in any way?

If life is present, is the tone of the cardia, poor though it may be, still enough to prevent entry of air?

Experimental evidence on the efficacy of expired-air resuscitation in people with full stomachs is lacking—quite rightly so since the danger is so great. Patients who have paralytic diseases requiring prolonged positive pressure breathing usually have intratracheal airways inserted.

Before advocating the general adoption of expired-air resuscitation, the question of regurgitation from the stomach must be clarified.

I should like to thank Dr. R. A. Goodbody, consultant pathologist, Southampton Group Hospitals, for permission to give some details of his postmortem report.

Esso Refinery,
Fawley,
Southampton. G. MATTHEWS.

A HAZARD OF PHOTOCOPYING

SIR,—As an industrial medical officer my attention was directed to an annotation in a business management journal which described a method of rendering paper more translucent for the purpose of photocopying by the dyeline process.

This annotation described how documents for photocopying should be wiped over with a solution consisting of trichlorethylene *B.P.* 2 parts; tricresyl phosphate 1 part; acetone *B.P.C.* $^1/_8$ part. It stated that this solution could be obtained at any chemist's shop.

The article described how the documents so treated will dry rapidly, thus enabling them to be photocopied. There was no warning about the use of this material, in spite of the fact that trichlorethylene is not only an anæsthetic but has been described as producing mental changes due to prolonged absorption, and is a drug of addiction.

The second ingredient, tricresyl phosphate, is not only equally toxic (if not more so than trichlorethylene) but is also a cumulative poison attacking the nervous system, and, what is most important, it is absorbed through the skin.

It is highly probable that in many offices and drawing offices where there is a need to photocopy letters, plans, and blueprints, photocopying has become a minor industry. It may well be that it is often carried out by young women who are probably ignorant of the hazards of this process. It is equally probable that, in an attempt to speed up the operation, the treated paper is held in front of a radiator or fire to hasten the drying process, and it is quite certain that the method described should be adopted only when steps are taken to ensure that no fume or vapour escapes into the atmosphere and none of the solution comes into contact with the operator's hands.

In view of the particular nature of the effects of tricresyl phosphate, it is most improbable that young women engaged on this work would be correctly diagnosed and more than likely they would go off sick after a period of some months' exposure, with a condition which might be mistaken, for example, for poliomyelitis.

During my investigation into this matter, I was also informed that an alternative method was to use a mixture composed of equal parts of carbon tetrachloride and castor oil. This seems an equally suspect process in view of the anæsthetic effects of carbon tetrachloride, and the same chronic effects on the kidneys and liver.

With the increasing adoption on office premises of mechanised equipment and technical processing of the kind described above, much of this work is probably carried out in the least suitable places—namely, an ill-ventilated basement.

At the present time there is, as your readers will know, a Bill before Parliament to safeguard the health, safety, and welfare of office workers. The control of working conditions in offices such as described, becomes not only desirable but probably lifesaving.

London, N.6. J. C. GRAHAM.

HUMAN RELATIONS IN OBSTETRIC PRACTICE

SIR,—Doctor's wives who read your journal will be grateful to Professor Morris for his timely and inspiring address and for Dr. Abraham's comment on it (April 30).

I am impressed by the fact that such an address should be needed. That such a state of affairs exists, and needs pointing out to doctors, is surely a reflection on the state of the healing art today. My own experience has been fortunate, in that I had my first baby in one of London's best obstetric units, and my second one in ideal conditions at home. Nevertheless I have seen and heard enough to convince me that the "sausage machine" approach to midwifery exists in the attitude of some of the nursing staff concerned with hospital confinements. At this most vulnerable period of a woman's life it only takes a small amount of impersonal and brusque handling to produce a considerable reaction; I am sure that Dr. Abraham's type of patient is not rare.

One does not expect doctors and nurses to be perfect, and although ideally Dr. Abraham may be right in advocating extensive teaching of dynamic psychology to those concerned, in the meantime is it not a matter of simple humanity to be able to remember that parturition is much less commonplace for the mother than for the experienced midwife?

London, S.W.19. CYNTHIA JACKSON.

SIR,—It is refreshing to see the note introduced by Professor Morris' article. Is it not time that all our hospital beds should be reserved for human people, members of families and of communities? For far too long have we been concerned with bed occupancy and the cost of an empty bed, but might not recovery be a little quicker (and dare I suggest more complete?) if the patients were treated generally in a more humanitarian fashion?

Is it really necessary for the pace to be so fast that no-one can be certain whether or not Mrs. X is definitely on tomorrow's list until after visiting hours? Wouldn't it be more reasonable to allow "someone" time to explain that "you may wake up with a tube running into your arm and another into your nose" and the reasons for the likely duration of these measures. Many people undergoing surgery have no idea where the scar will be. Surely a basic instruction to all who deal with people should be explain to the patient, *in terms he will understand*, what you are going to do and what he may expect as a result, and allow him an opportunity to ask questions if he wishes.

We talk about mental health and positive health, is it not time that we tried to estimate how much mental discomfort we as a profession may be responsible for?

I would add that these comments relate to the many frustrations I felt during the years I worked in hospitals because, for various reasons, I found myself unable to carry out these ideals.

Hadleigh, Essex. DAPHNE SASIENI.

MERIT AWARDS

SIR,—The letter of "Junior Medical Officer" (April 9) on the subject of merit awards prompted me to buy a copy of the Royal Commission's report. The figures he correctly quotes on the distribution of awards by specialty show all too well that a prophet is not without honour save in his own country. Over 55% of physicians receive awards: 51% of surgeons: 41% of obstetricians: of psychiatrists but 14% receive recognition: and anæsthetists are dismissed with a contemptuous 13%. This discrepancy is commented upon by the Commission itself (p. 82): and I understand that the leaders of the anæsthetists suggested to the Commission that the distribution of awards was rather low for this specialty.

Now these two apparently despised branches have one thing in common: in each case the value of the service rendered to medicine and to the community has greatly increased in recent years. I cannot speak on the international reputation of British psychiatry: but it is no exaggeration to say that, in the eyes of the world, British anæsthesia is unique: it is well ahead of any other country not only in the ability of the leaders, but also in its overall level. Postgraduates come from all countries to study anæsthesia here: the diplomas of the Faculty of Anæsthetists are the most prized in the world: and anæsthetic services established abroad are modelled on the English pattern.

It would be an insult to suggest that the Awards Committee may be unaware of the efflorescence of this branch of medicine. Since this cannot be so, then it is all the more important that the appearance of deliberate refusal of adequate recognition be rigorously eschewed. As justice has to be seen to be done as well as be done, so the very appearance of injustice must be avoided: most particularly when some of the near-Star-Chamber qualities of the administering body render it potentially suspect.

IN SOMNO PAUPERTAS.

TREATMENT OF SALICYLATE POISONING

SIR,—In your annotation of April 23 you state: "Continuous washing of the stomach is perhaps advisable, as salicylate may possibly be excreted into the stomach or be regurgitated from the small intestine during vomiting." This may perhaps possibly be as indecisive a remark as one can make, but aspirin poisoning is a common and dangerous hazard and deserves careful thought.

Professors Goodman and Gilman [1] are more forthright when they state: "It (salicylate) is not secreted in the gastric juice even at high plasma levels." They also maintain when discussing salicylate poisoning that the gastrointestinal symptoms, including vomiting, can occur without the appearance of salicylate in the gastric juice, and give references.

If this is incorrect, there are, as you suggest, obvious important therapeutic implications. You do not, however, give any reference in support of your statement, and before we discard other expert opinion, and particularly before we subject our patients, who are often toddlers, to repeated lavage, which is not without danger in a struggling vomiting baby, it is desirable that we should be allowed to examine the evidence on which you base your remark.

I feel rather strongly on this point partly because my resident was involved in the inquest you mention, where this point among others was raised, but mainly because your annotation might be regarded in some quarters as an authoritative expression of present opinion. If it were, and as some cases of aspirin poisoning will die whatever is done, further residents in the future may be criticised for not giving "continuous" lavage, which at the moment I personally regard as at best unnecessary. I am, however, open to correction.

Manor Hospital, Walsall. J. M GARVIE.

*** Our editorials seldom aim to review a subject exhaustively, and the one to which Dr. Garvie refers was not intended to deal comprehensively with the many opinions on the treatment of salicylate poisoning. We quoted Professor Webster's view but did not mean to imply that other opinions should be discounted. Many may feel, however, that continuous washing of the stomach is still advisable in the early stage of poisoning when salicylates would be expected to be present in the stomach and intestine. Goodman and Gilman's observations do not seem to weaken this first principle of treatment. We assure Dr. Garvie and his resident that we intended no criticism of the treatment in this particular case, for, as Dr. Garvie observes, some patients poisoned by salicylates will die whatever is done.—ED. L.

SIR,—Your annotation described the various methods which have been directed towards correction of the electrolytes in this condition. No mention was made, however, of the deaths which frequently occur due to respiratory failure, regurgitation of vomit, or exhaustion. These dangers are not always fully appreciated but their importance and prevention have been discussed by Freier et al.[2]

In the case which they described the boy had an initial blood-salicylate level of 66 mg. per 100 ml. He was intubated following an injection of *d*-tubocurarine chloride and controlled ventilation was maintained for 12 hours. After cessation

1. Goodman, L. S., Gilman, A. The Pharmacological Basis of Therapeutics; p. 291. New York., 1956.
2. Freier, S., Neal, B. W., Nisbet, H. I. A., Rees, G. J., Wilson, F. *Brit. med. J.* 1957, i, 1333.

of controlled ventilation the breathing was normal in rate and depth and there was no recurrence of tetanic spasms.

Intubation with a cuffed tube ensures that hypoxia is prevented and the obstruction of the relaxed tongue is bypassed. Furthermore, regurgitation of vomit is prevented so that tube-feeding may be instituted with safety.

Curarisation and controlled ventilation reduce the hyperactivity of the voluntary muscles and thereby reduce the probability of further disturbances in the electrolyte balance. Reduction of this hyperactivity lowers the hyperpyrexia so that death from exhaustion in small children is less likely to occur.

I believe, therefore, that treatment should be directed primarily towards restoration of the airway in those patients who are suffering from severe salicylate intoxication. When this has been achieved, attempts may be made to restore the normal electrolyte balance in the blood. It is difficult in some cases to decide when this method of treatment should be instituted, but once the patient begins to hyperventilate, the necessary anæsthetic equipment and drugs required for intubation and controlled ventilation should be at the bedside.

Celander and Haglund [3] have described three cases which were treated on similar lines by controlled ventilation through a tracheostome.

Southmead Hospital, Bristol. FRANK WILSON.

BLOOD-VOLUME IN ELDERLY ANÆMIC PATIENTS FOLLOWING BLOOD-TRANSFUSIONS

SIR,—I read with interest Dr. Andersen's article of April 2.

These studies conform with other work which suggests that the infusion of blood-plasma does not always or even regularly result in the anticipated expansion of the plasma-volume. Dr. Andersen has suggested that this phenomenon can be explained by "simple physicochemical forces which displace fluid and proteins from the circulating blood into the extracellular spaces spaces" thereby regulating the total blood-volume and the plasma-volume.

However, recent studies in man and animals deny the simple explanation offered by Dr. Andersen. Dogs were transfused firstly with autologous plasma which had been obtained from the same animals previously and held in the frozen state, and secondly with non-autologous or homologous plasma derived from other animals of the same species.[4 5] A dramatic difference was noted in the response of the same dogs to autologous and non-autologous plasma. An excellent expansion closely approximating to the anticipated value was obtained in almost all those dogs receiving autologous plasma. When, however, the same dogs received non-autologous plasma the expansion was frequently poor and in some cases an actual contraction of the plasma-volume was noted to occur in less than one hour following the infusion of plasma. Accompanying these transfusions (of non-autologous plasma) extensive urticaria was often noted. A fall in blood-pressure sometimes accompanied the cutaneous reaction. The evidence suggested that these reactions were due to a histamine release resulting from the infusion of plasma-proteins of a non-autologous donor. More recently we have duplicated these studies in volunteers.[6 7] Ten healthy individuals received approximately 500 ml. of autologous plasma which was held in the frozen state for at least a week before reinfusion. The increase in the plasma-volume was equal to 83% of the anticipated value. When fifteen healthy volunteers were infused with the same quantity of non-autologous plasma the mean retention, as determined by radioactive iodinated serum-albumin, was only 18%. Six of the fifteen developed urticaria during the infusion and four developed systemic reactions including headache, fever, chills, and nasal stuffiness. In general, a poor expansion of the plasma-volume was encountered in those individuals having severe reactions. No reactions were encountered in the recipients of autologous plasma. In all cases, the plasma-volume was determined one hour after infusion of the plasma.

It appears therefore that while some adjustment of plasma volume after transfusion is undoubtedly due to simple loss of plasma-protein from the circulation, a more important factor in clinical transfusion is the occurrence of plasma incompatibility leading to an increased capillary permiability.

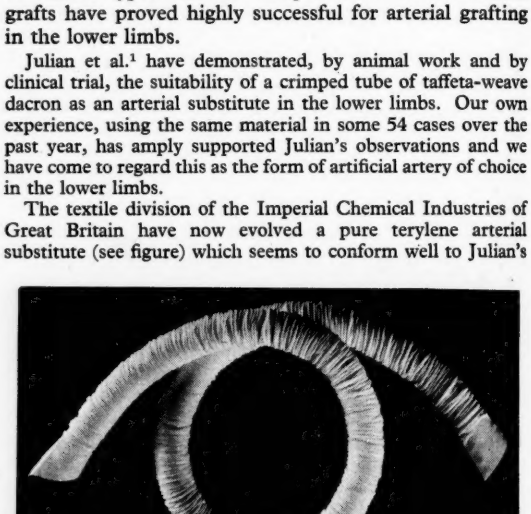
Montreal General Hospital. J. L. HUTCHISON.

A TERYLENE ARTERIAL PROSTHESIS FOR USE IN THE LOWER LIMBS

SIR,—The plastic fibre 'Terylene' was first developed in Britain by Imperial Chemical Industries, but it is also made, under licence, in the United States of America where it is known as 'Dacron'; recently this material has been used in America to construct arterial prostheses of various types. In the crimped forms these artificial grafts have proved highly successful for arterial grafting in the lower limbs.

Julian et al.[1] have demonstrated, by animal work and by clinical trial, the suitability of a crimped tube of taffeta-weave dacron as an arterial substitute in the lower limbs. Our own experience, using the same material in some 54 cases over the past year, has amply supported Julian's observations and we have come to regard this as the form of artificial artery of choice in the lower limbs.

The textile division of the Imperial Chemical Industries of Great Britain have now evolved a pure terylene arterial substitute (see figure) which seems to conform well to Julian's



recommendations; to distinguish this from the American product it is proposed to refer to it as "terylene arterial prosthesis", although we freely acknowledge our debt to our American colleagues for perfecting this form of plastic artery. The principal reason for developing a British terylene arterial substitute has been to reduce substantially the cost as compared with the imported dacron product.

The terylene arterial prosthesis has the possible advantage over the dacron counterpart that the lateral flanges characteristic of the latter have been abolished. Our impression is that the terylene graft is even more satisfactory than the dacron graft with regard to the ease with which the fabric is made blood-proof by pre-clotting.

The terylene arterial graft shows no appreciable tendency to fray when it is cut, and the crimping employed appears to give good protection against buckling when it is angulated. It is supplied sterilised by gamma-rays, but of course it can be boiled or autoclaved in addition; the manufacturers cleanse the material of any chemical contaminant before it is supplied. 8 mm. has been adopted as the standard diameter of this tubing because experience has shown that this will meet nearly all requirements in the lower limb; other diameters are available.

We have now used the terylene arterial prosthesis in 37

3. Celander, O., Haglund, G. *Acta anesth. scand.* 1958, **2**, 123.
4. Bliss, J. Q., Johns, D. G., Burgen, A. S. V. *Circulation Res.* 1959, **17**, 79.
5. Bliss, J. Q., Walker, J. D. *Canad. J. Biochem. Physiol.* 1959, **37**, 371.
6. Freedman, S. O., Bliss, J. Q., Hutchison, J. L., Burgen, A. S. V. *J. Allergy*, 1960, **31**, 134.
7. Hutchison, J. L., Freedman, S. O., Richards, B. A., Burgen, A. S. V. *J. Lab. clin. Med.* (in the press).

1. Julian, O. C., Deterling, R. A., Dye, W. S., Bhonslay, S., Grove, W. J., Belio, M. L., Javid, J. *Arch. Surg.* 1959, **78**, 260.

patients requiring a femoropopliteal arterial grafting procedure and the results have been observed for up to six months. This limited experience has shown that the terylene grafts possess all the excellent qualities of the American counterpart and should be capable of yielding long-term results equal to those reported by Julian. It is the purpose of this communication to draw attention to the availability of the British product, but it is our belief that the proper assessment of the procedures for which it is likely to be used will require some years.

Bifurcated abdominal grafts of similar material will be available shortly.

British-made terylene arterial prostheses may be obtained from Messrs. John Bell & Croyden, who also supply the imported American dacron arterial prostheses.

Royal Victoria Infirmary, Newcastle upon Tyne. D. J. TIBBS.
Hammersmith Hospital, London, W.12. PETER MARTIN.

MONDAY-TO-FRIDAY WARDS

SIR,—In your issue of April 30, Miss. Simpson suggests the possibility of Monday-to-Friday wards as a feature of hospital planning of the future. In the geriatric unit in this hospital, we have over the past few months been experimenting along these lines with certain of the longer-stay rehabilitation patients, as a logical extension of the principle of intermittent hospital care, of which the " six weeks in, six weeks out " scheme pioneered by Dr. John De Largy at Langthorne Hospital, E.11, is, a well-known example. We hope to report our experiences shortly, but in addition to easing the nursing load we feel it to be of value to this group of patients in particular, because it maintains their links with their homes and encourages the relatives to consider themselves part of a team responsible for the planning of long-term care of patients who might otherwise become depressing problems to themselves and their families, and indeed to the hospital staff who will ultimately have to care for them.

Ystrad Mynach Hospital, Hengoed, Glamorgan. MORAG L. INSLEY.

PAROMOMYCIN IN SHIGELLA AND SALMONELLA INFECTIONS

SIR,—I found the article of April 30 by Dr. Coles and his colleagues extremely interesting. I feel that if they had included more cases in which a chronic carrier state developed, refractory to other forms of treatment, due to salmonella infection, then the evaluation of paromomycin activity would have been easier. As we all know, this type of case is the one which is most likely to block valuable hospital cots and beds.

My experience in Fazakerley Hospital, Liverpool, using a different form of therapy, may be of interest. Under the guidance of Dr. A. B. Christie, I treated 10 children, between the ages of 18 months and 5 years, in whom the chronic carrier state due to *Salmonella typhimurium*, refractory to other forms of treatment, was well established with a combination of oral oxytetracycline (terramycin) (15 mg per lb. body-weight daily) and ' Enpac ' (3–4 g. daily) for five days. 9 of these patients were cured (three negative consecutive rectal swabs). In the 10th case two negative swabs were obtained and then the organism returned. These patients had all been previously treated with oral oxytetracycline and most had also received a course of oral streptomycin and sulphaguanidine.

A patient of 70 infected with *S. newport* was in hospital for nine months because of his chronic carrier state and the fact that he owned, worked in, and lived over a cafe. He was treated with a similar regime; and " cure " was obtained on two occasions using a criteria of six consecutive negative rectal swabs, but the organism always recurred on further testing. He finally sold his business and was then discharged from hospital.

I consider that this treatment is rational because the enpac supplies resistant lactobaccilli to replace the bowel flora disrupted by oxytetracycline.

St. Vincent's Hospital, Dublin. J. S. DOYLE.

FLUORIDATION

SIR,—The replies of the medical officers of health to Dr. Dobbs seem to show that we have to fight not only for pure water but for common sense in public-health affairs. Can *all* our public-health experts approve of imposing a general, indiscriminate, permanent increase in the intake of a well-known poison, and believe that the infliction of worry, indignation, and stress upon innumerable middle-aged people and invalids is the duty of the medical profession?

This insistence on coercion, and on a method which involves arousing the maximum possible public hostility, cannot arise from a sincere concern for the children's teeth; it is clear that the fluoridation campaign is being used, by those few who really know what they are doing, to break down the principles of consent and of individual care and treatment, which are absolutely fundamental to medicine and to public confidence in the medical profession.

WINIFRED M. SYKES
Secretary,
Huddersfield. National Pure Water Association.

HÆMORRHOIDS

SIR,—Your leading article of Feb. 20 on the treatment of hæmorrhoids and the correspondence which followed prompt us to record the results we have been obtaining with a comparatively new product. Although you recommend only injection or surgical removal, many milder cases do not warrant or the patient does not accept such treatment. Even in severe cases where hæmorrhoidectomy is contemplated, the patient's suffering must still be relieved during the waiting period.

Patients with hæmorrhoids of varying severity were given a supply of ' Proctosedyl ' (Roussel) suppositories and/or ointment (each suppository and each gramme of ointment contains 5 mg. hydrocortisone, 10 mg. framycetin sulphate, and 5 mg. cinchocaine). They were instructed to apply the ointment and insert a suppository morning and evening.

The results in 35 cases are summarised as follows:

1st degree hæmorrhoids: complete relief 14, helped 2, failed 1 (17)
2nd degree hæmorrhoids: complete relief 10, helped 1, failed 1 (12)
3rd degree hæmorrhoids: complete relief 4, helped 1, failed 1 (6)

Only 3 out of 35 patients received no benefit at all, but 32 received benefit of varying degrees, and 80% obtained complete relief.

Protoscopy was carried out at the first and subsequent visits to determine progress. All possible serious underlying diseases were also carefully excluded. The patients were followed for periods of several months and those who did not return for final assessment were excluded.

In fissure-in-ano results were also excellent, 4 out of 5 patients obtaining complete relief; but in the symptomatic treatment of pruritus ani, pruritus vulvæ, and vulvitis results were disappointing.

W. L. KERR
T. E. S. STOWELL
T. WADE WEST
Bitterne, Southampton. J. F. MULLAN.

SIR,—I have now treated approximately 50 patients with the preparation ' Alcos-Anal ', mentioned by Dr. Mustard (April 9), reserving it mainly for pregnant women with symptoms of hæmorrhoids, including slight bleeding.

Over 90% of patients stated that there was considerable relief of discomfort and even of pain, and that bleeding, when it occurred, was less than before treatment. No patient required injection or operation treatment after delivery, although at the initial postnatal visit, 2 patients looked as though they would need hæmorrhoidectomy. Three months later, the hæmorrhoids had considerably decreased in size with continued use of this preparation, which contains the sodium salts of unsaturated fatty acids of cod-liver oil.

The main disadvantage of this therapy is an unpleasant stinging sensation which lasts for about ten minutes after the ointment, or the pessary, has been introduced into the anus.

London, W.1. ELLIOT PHILIPP.

BRONCHOGRAPHY

SIR,—I read with interest the article of March 5 by Dr. Smith and his colleagues. I cannot agree with their contention that "A trained assistant is necessary to position and support the patient . . . normally a physiotherapist." I use a much simpler method which gives excellent filling.

The patient, after insertion of the tracheal catheter, is placed on the X-ray table which is tilted 5°–10°, feet downwards. The patient reclines at an angle of about 45° with the side to be filled lowermost and the head well supported on a couple of pillows. The patient hyperventilates half-a-dozen times and then holds the breath in full expiration. The dye is injected down the catheter as rapidly as possible (16–18 ml. suffices for each side in an average adult) and the patient is then instructed to breathe in normally. Films are taken immediately, erect or supine as desired. With a little experience, this technique gives consistently uniform filling of all lobes on the side being investigated.

Incidentally, this method is readily adaptable to bronchography under general anæsthesia. This is performed with a short-acting relaxant, and the dye is "pushed out" into the bronchi by manipulation of the anæsthetist's bag, which at the same time keeps the patient oxygenated.

I do not claim originality for this method, but merely wish to draw the attention of Dr. Smith and his colleagues and others interested to a much quicker and simpler method of performing bronchography both under local and general anæsthesia.

Hobart, Tasmania. JOHN BLOOMFIELD.

IMMUNE TOLERANCE IN MOTHER AND FŒTUS

SIR,—It is strange that Dr. Galton (Feb. 27) should state that no account has been taken of the antigenic action of the placenta.

Medawar [1] as far as I am aware first discussed this problem. I pointed out [2] the extraordinary inconsistencies that inevitably arise when syncytiotrophoblast is considered of fœtal origin, and suggested, as a reasoned solution, that the problem really did not exist since the tissue concerned may well be maternal of granulosa-cell origin. Since then discussion has ranged wide and speculation almost equalled that of the schoolmen who argued how many angels could be present on the head of a pin. Dr. Park (April 16), as he indeed points out, recently discussed this problem, but he does not mention that of the three solutions he posed, he found none satisfactory; the last of the three was that the trophoblast differed antigenically from the rest of the fœtus of which it is said to be part. Unlike Dr. Galton, he finds difficulty in accepting this solution.

This placental tissue, according to various contenders, is primitive, or highly specialised; antigenically simple, or complicated; ectoderm, mesoderm, entoderm, or all rolled into one as "protoderm". It produces the hormones of the pituitary, ovary, adrenal, and endometrium of the mare, and thus contains within itself both the conductor and players of the hormone orchestra. The nuclei are haploid without Barr chromatin bodies or polyploid with them. It is a cancer and it is not, and when without a doubt it is a cancer as chorionepithelioma it invades another individual, the mother, but not the fœtus of which it is part. Derived from the fœtus, it has an existence apart from it, as in the hydatidiform mole. The theory of recapitulation (which states that an individual in its embryonic stages recapitulates the life of the species), although somewhat rusty these days, is turned upside down. And so on! All these difficulties cease to exist if the syncytiotrophoblast arises from granulosa cells and its function is to protect fœtus and mother from each other antigenically.

Should Dr. Galton succeed in demonstrating that syncytiotrophoblast nuclei are haploid the hypothesis I have suggested would not be invalidated unless the granulosa cells surrounding the ovum did not have haploid nuclei. To add to the current speculation, if these latter cells have haploid nuclei they could be parthenogenetic twins (or rather multiplets) of the fertilised ovum.

Public Health Offices, Ilford. I. GORDON.

1. Medawar, P. B. *Quart. J. micr. Sci.* 1948, **89**, 239.
2. Gordon, I. *Lancet*, 1949, i, 807.

A PORTABLE FREE-FIELD AUDIOMETER

SIR,—The exchange of views on the free-field audiometer (April 16) raises problems in audiometry which are worth discussing in detail.

Mr. Ashton restated some well-known acoustic principles concerning audiometry when earphones are used and contrasted this with free-field audiometry when poor acoustics can reduce the accuracy of the measurement. The use of earphones makes the measurements independent of the sound-reflecting quality of the room but *not* independent of other conditions and qualities of the room. In fact, *conditions under which tests are frequently carried out* are one of the major sources of error in audiometry. You may have a good machine in a perfectly acoustically treated room, but if it is an unventilated small *cubicle* in which both the subject (mainly when a child or elderly person) *and the examiner* suffer acute discomfort, the result will be frequently a false one. If you add to it an inadequately trained audiometrician (unfortunately still a very frequent occurrence) who does not use a standardised procedure, the result will be wide of the mark. This still happens again and again. It is not so much the machine or lack of acoustic treatment of walls which leads audiometry into disrepute, but lack of suitable conditions and thorough training of audiometricians (mainly in testing children). This is a pity, because undoubtedly pure-tone threshold audiometry is still the best single test which informs us about the physiological condition of the hearing apparatus.

It is high time it was realised that audiometric tests cannot be carried out satisfactorily in small, miserable, unventilated cubicles. A cubicle or any unfriendly poky little room is entirely unsatisfactory for this important subjective hearing test.

Physical standards for the machines have been worked out but we still lack standardisation of satisfactory conditions for the test, and even standardisation of technique.

Audiometry in children requires a good-sized, pleasant, and comfortable room in which play audiometry, using conditioning methods, can be carried out. I have found the Denes-Reed free-field audiometer particularly useful in preparing a small child for full threshold audiometry.

The child is first conditioned, in free field, with an interesting sound. Then the play continues with pure notes, with the help of the free-field audiometer. At this stage I introduce a transitional step. Initially, many children may be reluctant to wear large earphones, so I use a single earphone, unattached to a wire, which has a transistorised oscillator incorporated in it. This produces a moderately loud single note when a spring is pressed, and the earphone is slowly moved towards the child's ear until it rests on the auricle. Probably he will now tolerate the large earphones more readily and can be transferred from free-field testing to more accurate threshold audiometry.

In addition it must be remembered that earphones are designed for adults. Frequently they are too big and cumbersome for the head of the small child. No manufacturer of audiometers has yet thought to provide earphones and headbands designed primarily for children. Inaccurately fitting earphones will invalidate results obtained from the best machine under perfect acoustic conditions.

Harrow. L. FISCH.

NOT TOO BIG

SIR,—From your editorial (April 30) on the psychiatric hospitals of the future I note that a bed complement of 300 is suggested to keep the hospital sufficiently small. It would be interesting to know the size of the population for which it is intended to cater. In the Manchester region, fully comprehensive psychiatric departments in a general-hospital setting are being built up, and I think we are discovering—somewhat to our amazement—how few beds are in fact needed if the department is properly organised.

My own department (which is in a general hospital) has 99 beds and serves a catchment area of some 254,000. Though at this stage I cannot give actual figures, I can safely say that, at a conservative estimate, it is coping with at least 85% of all inpatients. This assumes that the beds are not blocked by subnormal patients, that there is an active and cooperative geriatric department in the hospital group, and that so-called community mental health services are fully organised. If these provisos are met, I am left with the strong impression, on the basis of actual experience, that fewer psychiatric beds are needed than might be thought necessary on a-priori grounds.

Blackburn. MAURICE SILVERMAN.

PREVENTION OF SERUM HEPATITIS

SIR,—In your annotation of April 16, you say that "donors with a previous history of jaundice are unacceptable". This can hardly be correct, partly because jaundice may be due to proven cholelithiasis, and partly because of the studies of Matthes and Riderer.[1] They studied the frequency of inoculation hepatitis in recipients who had received blood from donors with hepatitis at different times before the bleeding. They came to the following results:

Of 85 transfusions with blood from donors who had suffered from hepatitis six years or more before the bleeding 3 (3·6%) gave rise to hepatitis in the recipient. Of 30 transfusions for which the corresponding interval was 3–5 years 2 recipients (6·3%) developed hepatitis, and for the intervals 1–2 years, 7–12 months, and 3–6 months the corresponding figures were 24 and 2 (7·8%), 19 and 2 (10·2%), and 3 and 2 (66·7%). The proportion of hepatitis among recipients receiving blood from donors *without* a history of hepatitis was found to be 4·2%—i.e., of the same order as for donors with hepatitis 6 years or more before the bleeding. As everyone who is responsible for obtaining sufficient blood for a hospital will know, it is hard to get sufficient donors, and it therefore seems to make things unnecessarily difficult to exclude all donors with previous jaundice, when well-documented investigations clearly show that donors with hepatitis more than 6 years back are not more dangerous than donors without a history of hepatitis.

Concerning the interesting paper of Bang et al.,[2] referred to in your annotation, it is important to remember that of the donors tested for S.G.O.T. 23·2% had values above 40 Wroblewski units, 12·5% had 50–100 units, and 2·1% above 100 units. If S.G.O.T. should function as a screen test for eliminating donors it would therefore be quite unrealistic to use 40 Wrobleswki units as the limit, and if 100 units is to be used as a limit the whole matter seems rather problematic. In my opinion the results of Bang et al. show that S.G.O.T. is not usable as a screen test for eliminating hepatitis carriers among donors.

Svendborg, Denmark. TORBEN K. WITH.

1. Matthes, M., Riderer, U. *Dtsch. med. Wschr.* 1956, **81**, 1914; *Germ. med. Mon.* 1957, **2**, 107.
2. *J. Amer. med. Ass.* 1959, **171**, 2303.

AN EASIER ALPHABET

SIR,—So many issues (and a few dubious arguments) have emerged in the discussion of redundancy that some ends are bound to be left untied. May I however make an attempt to show how some of them may be woven into a coherent pattern?

There seems to have been some confusion between the concepts of "redundancy" and of "noise". If we imagine an ideally simplified alphabet and then add to each of the letters a *different* "curl, ball or spike", we are making the letters more specific; since this is not strictly necessary, the added information is redundant. If on the other hand we add *the same* ornament to each and every letter we are making the letters more complex but not more specific. The ornament is worse than useless, for it obscures the differences between letters—it is "noise". Noise, which is *irrelevant* information, must be distinguished from redundancy, which is *superfluous relevant* information; the former is always noxious, the latter always potentially protective.

Now in the card-sorting experiment it was shown that when the cards differed in colour, shape, and size, but were sorted only according to colour, certain illiterates were unable to ignore the shape and size differences and would work at a rate corresponding not to 1 bit/card but to 3 bits/card. From this it was very reasonably inferred that the irrelevant information concerning shape and size was retarding their performance. It would be more consistent to go on to say that performance was retarded because the brain was *unable to exclude noise* than to incriminate redundancy.

According to the usual electronic analogy, an efficient brain has an intrinsically high signal/noise ratio and is therefore able to pick out a signal from a background of noise. Returning to the idea of a "noisy" alphabet, above, it will be clear that a reader who recognises that the same ornament is present in all the letters has taken the first step towards ignoring it. His brain must be able to discriminate, and become selectively accommodated to, any invariant characteristic of all the letters. A brain which lacks the ability to detect the "highest common factor", and becomes unresponsive to it in this way, will have to continue handling each letter whole instead of "recognising" it by a minimal number of cues. My feeling is that Dr. Pugmire's card-sorting experiment (April 23) has really revealed a low signal/noise ratio for visual perception in certain illiterates and that noise rather than redundancy is the evil of which we should seek to rid our language, not only its alphabet, but at all levels. It is precisely when the communication system has a low signal/noise ratio that redundancy in the signal has its greatest protective value, hence my remark: "It may be that redundancy in the script is only protective . . . where the defect lies in the perception and recognition of printed symbols, rather than in the comprehension of words."

Perhaps it should be made more explicit that just as the addition of extra specific detail to letters is a redundancy which protects primarily against the misidentification of *letters*, so the presence of seemingly superfluous letters in a word is mainly a guard against misidentification of the *word*; similarly for the presence of "superfluous" words in a sentence, sentences in a paragraph, and so on. So long as the extra matter is relevant, a certain amount of repetitiousness is valuable; especially is this so in printed language, where no information can be conveyed, nor can the attention of the audience be ensured, by the devices of intonation, facial expression, and gesture, which are so important a part of speech.

Finally, I would assure Dr. Jarrett (April 23) that the word "cough" does illustrate the general principle that "redun-

dancy protects". Consider the misprints arising from error in any one of the three letters "ugh". The only two words with which "cough" could be confounded are "couch" and "couth". If, however, the word were normally spelt "cof", misprinting of the letter "f" could result in no fewer than ten distinct words. The "ugh" spelling reduces the ambiguity caused by a misprinted letter. That this ambiguity is not merely an academic abstraction may be seen from the devastating effect of misprinting "cough" in the famous *sloca* which I will proceed to relate:

> "It wasn't the couch that carried him off
> But the coffin they carried him off in."

The distinction between redundancy and noise does not only bear upon the relatively abstruse problems of language statistics but also upon the intelligent management of every communication task. It might be summed up, perhaps, in the advice "Repeat yourself if necessary, but stick to the point".

London, W.1. H. B. G. THOMAS.

THE COMPREHENSIVE HANDBOOK ON PRESCRIBING

SIR,—A new handbook with this title has been issued this week to all practitioners on the National Health Service list. It is a most sumptuous edition. There is as far as I could see nothing new in it not already covered by previous publications. The outdated 14-pin binder is not the easiest to handle, but obviously no expense has been spared. It is provided with a pocket for the *National Formulary*, which might be useful if it could enter it.

We are told in the first paragraph of the green section that we are "expected to exercise reasonable care in avoiding waste of public funds". Were ever so many before told to do this in so expensive a manner?

Thornton Heath. B. DE BURCA.

RESISTANT ASCITES TREATED BY COMBINED DIURETIC THERAPY

SIR,—The interesting observations of Dr. Shaldon and his colleagues (March 19) on the additive diuretic effect of mannitol administered in combination with spironolactone (SC-9420, 'Aldactone') for the treatment of resistant ascites may have failed to adequately emphasise the contribution of the aldosterone antagonist in promoting loss of ascitic fluid.

Our experience[1] in eight patients with cirrhosis and refractory ascites treated with spironolactone after appropriate control periods showed a remarkable response in every case. The clinical response in terms of loss of fluid was not apparent until the drug had been administered for periods of 2–5 days, and then was stepwise and progressive for several days thereafter. Early experience using total daily dosages of 400 mg. indicated this dosage was often inadequate, and the optimal dosage among our patients was 600–800 mg. daily.

The addition of mannitol on the second day of treatment with spironolactone may coincide with the beginning of the clinical response to this drug and the effects of any additional therapy would then be inseparable.

In our observations[2] on four patients, the addition of mannitol (2 litres 10% solution administered intravenously) to spironolactone, after the latter had been given continuously for 5 days using a total daily dosage of 800 mg., was not followed by an increase in the volume or sodium content of the urine above that found during the administration of aldactone alone.

Our studies indicate that the resistance to diuretics, encountered in patients with cirrhosis and ascites, is due in a large part, if not entirely, to hyperaldosteronism and that adequate treatment antagonising the effects of aldosterone will, by itself, induce diuresis. The disadvantages of administering mannitol intravenously would additionally appear to lessen its usefulness in the long-term management of patients with cirrhosis and resistant ascites.

B. F. CLOWDUS
J. A. HIGGINS
J. W. ROSEVEAR
W. H. J. SUMMERSKILL.
Mayo Clinic, Rochester.

1. Clowdus, B. F., Higgins, J. A., Rosevear, J. W., Summerskill, W. H. J. *Proc. Mayo Clin.* 1960, **35**, 97.
2. Clowdus, B. F., Higgins, J. A., Rosevear, J. W., Summerskill, W. H. J. Unpublished data.

THE PERSONAL DOCTOR

SIR,—The vexed questions whether the general practitioner should be a "personal doctor" or whether he should be one of a large specialising group practice, whether he should work from his house or from a central clinic, or whether he should even exist at all, affords much thought for speculation and argument; but the fact remains that we are committed to a general-practitioner service and it behoves us to seek ways to make it as efficient as possible. To my mind, paradoxically enough, it is the specialists who can be of most help.

The value and status of the G.P. will never be at its best, or anywhere near it, until the specialists see that the hospital service and the G.P. service work as one. When the G.P. has facilities for diagnostic aids on direct application and has at his disposal G.P. hospital beds, as well as the use of a minor-operation theatre and ample opportunities for clinical assistantships in outpatient departments, then, and only then, can he give of his best and take a reasonable part in the Health Service of this country. At the moment, in most parts of this country he is denied all these things.

Even those who have higher degrees or those who show proof of special experience in a specialty (e.g., hold a diploma) can find no outlet for this experience, and it seems that most consultants are determined that they never shall.

Many reasons for this attitude spring to mind but heated discussion of them would lead nowhere, and I am sure in the long run that, if only the specialists would open up their closed shop, they themselves would also benefit, because they would be really seeing only those cases that needed a specialist's opinion. The public would also benefit and it could well be that the cost of the Health Service might be lowered.

London, S.W.11. IAN SAMUEL.

PREVENTION AND TREATMENT OF BEDSORES

SIR,—I feel that Dr. Pathy (March 12) has rightly stressed that, even at an early stage of a pressure sore, necrosis has extended to fat and muscle, and that this emphasises the greater importance of turning a patient than of local applications.

It has been suggested[1] that the devitalised atrophic tissues of an elderly patient may actually suffer damage when rubbed with spirit or other preparations.

With this in mind, a number of bed-fast, and mostly incontinent, patients in a geriatric ward had their pressure areas and sores routinely treated with the following silicone preparation, in the form of an ærosol spray:

Aluminium dihydroxyallantoinate	0·5% w/v
Cetyl pyridinium chloride	0·1% w/v
Terpineol	1·0% w/v
Silicone fluid	ad. 100%

The aluminium dihydroxyallantoinate and cetyl pyridinium chloride are suspended as finally micronised powders.

In addition to the water-repellent and protective properties of the silicone compounds, the spray combines the astringent and bacteriostatic action of aluminium with the healing properties of allantoin. Cetyl pyridinium chloride possesses bactericidal properties, and terpineol is a pleasant-smelling antiseptic.

1. Bateman, F. J. A. *Brit. med. J.* 1956, i, 554.

The original formula contained liquid paraffin, but as this prolonged the drying time it was omitted.

Only a momentary pressure on the aerosol spray button was required to deliver a film of silicone fluid on to the patient's skin. Unless fouled, the skin was washed infrequently, and the patient's position changed as often as possible.

It was felt that the incidence of bedsores had been reduced. The nursing staff was enthusiastic about this method of treatment, for æsthetic and time-saving reasons. Compared with the old methods of rubbing with spirit, &c., the patients were spared unnecessary discomfort, and the simplicity of the aerosol method would suggest its suitability for use in the home-nursing of the elderly, in colostomy hygiene, and the prevention and treatment of napkin rash.

Chorlton-cum-Hardy, Manchester. H. H. D. KELLY.

ORAL HYPOGLYCÆMIC AGENTS

SIR,—Dr. Henry Dolger's experiences with chlorpropamide have been so unfortunate and so different from those of others on this side of the Atlantic, including our own, that one is tempted to doubt whether the high incidence of jaundice reported by him in his letter of April 30 can be entirely attributed to the use of this drug.

In the small series of cases reported by us [1] there was no instance of jaundice, and this complication has not been observed in any of the much larger number of patients at present receiving chlorpropamide in our diabetic clinic. The total incidence of jaundice in patients receiving chlorpropamide therapy in the United Kingdom is 0·02%.

Even more surprising are his remarks on hypoglycæmia which would not appear to be a manifestation of idiosyncrasy and which we have encountered only rarely and almost always in a mild form using the regime described in our article.

In some early trials of chlorpropamide [2] there was a significant incidence of toxic effects, now recognised as being due to overdosage; the high incidence of severe hypoglycæmia and jaundice reported by Dr. Dolger suggests the possibility that the use of this drug in more than therapeutic doses may have been the responsible factor.

Before condemning chlorpropamide as a significant cause of jaundice, Dr. Dolger should present some good reasons for regarding it as being a propter rather than possibly just a post hoc manifestation; Graham [3] reported a number of cases of jaundice occurring in a diabetic clinic long before the days of the oral hypoglycæmic drugs, the only common therapeutic agent being insulin.

No doubt Dr. Dolger will be publishing the detailed findings in the two cases which developed jaundice on chlorpropamide in a daily dose of 250 mg.; in the meanwhile it will be unwise to draw conclusions from his remarks.

The Diabetic Clinic, King's College Hospital, London, S.E.5. W. G. OAKLEY D. JACKSON.

PALLIATION OF MALIGNANT STRICTURE OF THE ŒSOPHAGUS

SIR,—I agree with Mr. Moghissi (March 26) that the Mousseau-Barbin tube is a very useful means of palliation of malignant œsophageal stricture.

I was very interested in the remarks of Mr. Jamieson and his colleagues (April 23), who report two cases in which the upper "funnel" end of the tube eroded the wall of the œsophagus. I have not myself encountered this complication, but have been aware of the possibility, and for some time have cut off a considerable portion of the rim of the funnel (which is coloured blue) in order to reduce its size. Is the English œsophagus less capacious than the French, one wonders?

It is important to insert as large a tube as conveniently possible in order that it may be pulled down and jammed well into the growth. This manœuvre is, I think, best controlled by following the passage of the tube through an œsophagoscope. If the tube is pulled down too far the funnel will kink and itself cause an obstruction.

In my experience the Mousseau-Barbin tube provides by far the best palliation for an inoperable cancer of the œsophagus. Souttar's tubes are often dangerous to insert, and tend all too frequently to slip through the constricted area. It may also usefully be inserted at thoracotomy when a growth proves to be unresectable.

Finally, one has to remind oneself that palliation of a malignant stricture is not curative, and one should not expect too much from any one method. Relief of the distress of extreme dysphagia should always be achieved whenever possible, but it seems to me that one must beware that one does not merely substitute for it a more prolonged agony. Sometimes heavy sedation alone can be more merciful for these unfortunate patients. The decision is often very difficult.

Liverpool. B. J. BICKFORD.

1. Jackson, D., Oakley, W. G. *Lancet*, 1959, ii, 752.
2. Walker, J. *ibid.* 1958, ii, 641.
3. Graham, G. *ibid.* 1938, ii, 1.

Parliament

Royal College of Physicians of London

ON May 9 at the second reading of this Bill Dr. BARNETT STROSS moved its rejection,[1] though he sympathised with its objects. He did so to obtain time for a debate on the constitution of the college. It was not his intention to dictate to the college, but he asked it to think again about grievances felt by many of its members. One of these was the procedure for the election of fellows.

Fellows, he explained, were elected, or, as some people felt, selected, from the members, but they were elected only by the existing fellows and not by members. Members could be put forward for fellowship only by other fellows and not by a member. The list of those who were so sponsored did not reach the council of the college directly. Two committees screened the names. Members did not think it reasonable that when their names were put forward in the ordinary way by fellows for a fellowship their names should not go forward directly for ballot.

The fellowship was an important and graceful distinction; but there was another implication, too, for members told him that in their view merit awards more easily followed fellowship. Therefore, they felt nervous of criticising the constitution of the college or the method of election for fear that they would become unpopular. The 4000 members had two representatives on the council of the college. Neither they nor any of the members had complained about the method of election to the fellowship. Dr. Stross found it alarming that the officers of the college should have no knowledge that there was any feeling about the matter.

What was even more archaic was that a fellow had no vote unless he was present in person in London at the headquarters of the college. Dr. Stross understood that a normal attendance at a meeting was about 90; thus 10% of the fellows elected officers or fellows and made decisions. Fellows who were in the provinces were at a disadvantage, and the many fellows scattered all over the world virtually could not vote at all.

In response to an interjection Dr. Stross said that he had received 8 letters from members. He had been asked by members to say that they should have some right of government and, therefore, should have a vote. They also thought that even if they did not have a vote, the fellows, at least, should have a postal vote.

Sir WAVELL WAKEFIELD said that among all the letters he had received about the Bill, none contained a single complaint or grievance, but he realised that that did not mean that such grievances did not exist. He hoped that the words said in the House would be seriously considered by those responsible for the running of the college.

1. See *Lancet*, April 23,1960, p. 912.

Mr. KENNETH ROBINSON accepted that the college was a most distinguished body which had a long history of service to medicine in this country. Nevertheless, it could not conduct its affairs totally insulated from the world outside. He was in favour of a postal ballot among fellows, and he could not see any reason why members should not join in electing the officers of the college and perhaps of the council. He did not think that 2 councillors out of nearly 4000 members was a fully adequate representation. It was odd that no complaint had ever reached the college. It was plain that so much depended on the decision of the hierarchy of the college that members would be rash indeed to voice their criticisms too loudly. Criticism that he had heard had not been confined to members. Indeed, fellows had said that they thought that it was excellent that a debate should take place in the House and that the structure and constitution of the college should come under review.

Sir MALCOLM STODDART-SCOTT pointed out that to become a fellow was to receive an award for academic distinction. That could be done only by selection. It could not possibly be done by election. Dr. Stross had expressed the dissident and dissatisfied views of 8 members of the college. There would always be somebody who fell below the line and would be dissatisfied and wish to have some other method of choice of fellows.

Dr. J. DICKSON MABON said that we must not pretend that because the college had a great record it was completely without any defect that could be altered to make matters more in tune with the times. No member was said to have complained to the college, but 12 had spoken to him and 6 had written. He now understood why these people did not wish to go into print. It smacked very much of an oligarchy dispensing patronage, that one must not offend. Something was seriously wrong when men of medicine should be unable because of fear of their own incomes, position, or future prospects to speak up and make radical constitutional changes within their own organisation. The college had categorically and officially refused to consider any reform of its constitution and practice. That sort of self-satisfied, smug attitude was a wrong way for a distinguished college to conduct itself.

Miss EDITH PITT, parliamentary secretary to the Ministry of Health, said that the objects of the Bill were unexceptionable and were greatly desired by a most respected section of the medical profession. The opposition to the Bill had been based on matters which were not connected with the Bill in any way—namely, what was alleged to be the undemocratic attitude of the college, and particularly the way in which the fellows were selected from the members and the rule that members of the college were not allowed to vote in the fellowship election. Whether they were justified or not, they had nothing to do with the merits of the Bill and they should be pursued within the profession. The Minister understood that there was machinery which would enable this to be done. Dr. Stross thought that the machinery was extremely limited. Nevertheless, the Ministry were advised that there was a vehicle through which these protests could be raised in the council by the standing committee of members. The issues which had been raised by some members had no bearing on the matters contained in the Bill, which everyone felt were admirable. She hoped that its purpose would not fail because of a discussion quite outside its province.

Dr. STROSS said that he hoped that the college would study what had been said, and withdrew the amendment.

Professions Supplementary to Medicine Bill

At the report stage on May 4, Mr. DEREK WALKER-SMITH honoured the undertaking which he had given at the second reading and moved amendments excluding speech therapists from the Bill. The speech therapists continued to object to their inclusion, and he was sure that inclusion should be regarded as a privilege and not as a penalty and that entry should be by way of conviction and not compulsion. The amendment would affect the composition of the Council to be set up by the Bill. To maintain numerical equality between the representative members and the medical members, the 8 medical members must be reduced to 7. He proposed to do this by reducing the number of members appointed by the Minister of Health from 4 to 3 and to provide that of these only 1, instead of 2, must be a doctor.

Though the statutory powers of subpœna which were originally in the Bill had been omitted by decision of the House this did not mean that the disciplinary committees would have no powers of subpœna. Such committees exercised a jurisdiction of a judicial nature and were generally recognised as constituting tribunals, and the Supreme Court had at all times lent its aid to inferior tribunals where they themselves lacked the means of enforcing the attendance of witnesses. If, as a result of the report of Lord Simonds' Committee, amendments fell to be made to the Bill in another place, they would come back to the House in the ordinary way of procedure. If the report called for legislation in a wider and more general field than these supplementary professions, then that general legislation would govern the proceedings of these committees, albeit under the terms of a general Act and not under the terms of this Bill. It was obviously bound to be some time before the Council and boards were set up under this Bill, before the initial registers were prepared, and before the disciplinary committees were functioning. Before that time the matter could be dealt with in whichever way was appropriate.

QUESTION TIME

How Many Patients?

Mr. L. A. PAVITT asked the Minister of Health what review was being undertaken in his department of the maximum number of patients permitted for a general practitioner in the National Health Service, with a view to the formulation of policy on this matter prior to the negotiations with the medical profession arising from the Pilkington report.—Mr. DEREK WALKER-SMITH replied: The general medical services are constantly under review in consultation with the medical profession so that any need for improvement or modification may be revealed and dealt with as opportunities occur. Mr. PAVITT: Does the Minister realise that it is impossible for a G.P. with a maximum list of 3500 patients to give a high standard of medical care? That means that he has an average of 17,500 consultations a year. If he works 365 days and takes in Christmas day and holidays as well, this works out at more than 50 consultations a day. Is it not time that some bold initiative was taken by the Minister to couple the awards that the Pilkington Commission recommended with some improvements in general practice?—Mr. WALKER-SMITH: It is always important to try to achieve whatever improvements in general practice we can, and it may be that this matter of maximum lists could arise in the context of discussion in regard to distribution. I would remind the hon. Gentleman that he is going on the basis of the maximum list, whereas the average list is only 2282.

Mr. KENNETH ROBINSON: Will the Minister go a little further and say that he himself or his representatives will raise the subject of the desirability of reducing doctors' lists when he discusses with the profession the distribution of the central pool?—Mr. WALKER-SMITH: It is a little early to anticipate the trend of the discussions which we shall be having with the medical profession, but I will certainly bear in mind what the hon. Member has said.

Pilkington Recommendations

Dr. DONALD JOHNSON asked the Minister to what extent the acceptance by the Government of the recommendations of the report of the Royal Commission as they stand, provided the doctors and dentists accepted them on the same basis, embraced the proposal for a special fund of £500,000 for differential payments to general practitioners; and whether, in the light of the controversial nature of this proposal, he would make it a matter for separate negotiation from the main body of proposals.—Mr. WALKER-SMITH replied: Full acceptance of the Royal Commission's recommendations necessarily includes acceptance of the award proposals for consultants, but not the creation of a special fund for differential payments

to general practitioners which would depend, as recommended by the Royal Commission, whether a scheme was agreed for its application. The distribution of the central pool would as hitherto be a matter for agreement between the Government and the profession.

Mr. KENNETH ROBINSON: Is the Minister aware that the misgivings which have been expressed by hon. Members opposite and by the profession about the merit awards for general practitioners are shared by this side of the House? Can he say why he took the step of announcing his acceptance of these recommendations as a whole before canvassing the views of the House? Is he aware that many of us have views on the matter which he might find helpful in his discussions with the profession?—Mr. WALKER-SMITH: The Government's offer to accept the report as a whole if the professions would do the same seemed to us to be a proper and equitable way in which to approach the matter. If the hon. Gentleman has in mind any proposals in the report which he thinks ought not to be followed, no doubt he will say so. Our approach is that neither side should pick or choose the bits which happen to suit it best.

Salaries of University Teachers

IN a written answer Mr. HEATHCOAT-AMORY said that he was satisfied that a revision of the salaries of academic staff at the universities was now necessary if regard was to be had both to salary increases in comparable professions and to the need to retain and recruit staff of adequate calibre during the forthcoming period of great expansion in the universities. He had considered the University Grants Committee's recommendation for non-medical and preclinical staff, and he proposed to ask Parliament to provide the additional funds required to enable the universities to bring into effect, as from Jan. 1, 1960, the following revised rates and scales of salary for full-time academic staff:

NON-MEDICAL POSTS

Professors

Basic salaries of £2600 a year, with provision for supplementation allowing for a range of salaries up to £3600 a year.

Readers and senior lecturers

A range of salaries with varying maxima up to £2425 a year, or in special circumstances to £2525 a year.

Lecturers

Scales rising generally from £1050 × £50–£1400 × £75–£1850 a year.

Assistant lecturers

A scale rising from £800 × £50–£950 a year.

PRECLINICAL POSTS

Professors

Salaries ranging from £2600 to £3600 a year.

Readers

Salaries within the maxima indicated below for lecturers.

Lecturers

Scales of salary rising from £1050 × £100 to maxima ranging from £1850 to £2525 a year.

The total consequential increase in the recurrent grants of the universities was estimated to be about £3½ million a year initially. The U.G.C. were considering the position of clinical staff in relation to the conclusions of the Royal Commission and would in due course submit recommendations for them.

Government Doctors in Malta

Mr. J. D. CRONIN asked the Secretary of State for the Colonies if he would make a statement on the circumstances of the recent strike of doctors in the Government service of Malta.—Mr. IAIN MACLEOD replied: The strike arose over the appointment of a new deputy senior medical officer, and the administrative channels for dealing with the affairs of the Medical Department within the Government Secretariat. The Medical Officers' Union advised the Government on April 30 of its intention to strike as from midnight the following day, without previously giving any notice of the existence of a dispute. An emergency medical service is operating. Mr. CRONIN: Was not this strike precipitated by the circumstance that the Government appointed a deputy senior medical officer contrary to the recommendations of the Joint Advisory Board? Was not this an act which showed a considerable lack of administrative tact, having regard to the general political situation and to the discontent which has been present in the medical profession there for many years?—Mr. MACLEOD: With respect, I think that is only half the story, because the Government were also advised by the Public Service Commission to appoint the man whom they did appoint, and, in spite of the advice of the medical board that the post should be advertised, the Government felt that was not a proper thing to do for an adminstrative post, and that ordinary promotion should carry on. That is what the Government did.

Corneal Grafting

Lord STONHAM asked H.M.'s Government whether they were aware of the urgent need for cadaver eyes for corneal grafting and of the long waiting-list of patients requiring this treatment; and if, in the hope of increasing the number of donors, they would, through the publication of an explanatory leaflet, seek to inform the public of this need.—Lord ST. OSWALD replied: Inquiries made of hospital boards last year showed no general shortage, but some notable local difficulties. In the view of the Government these needs are best met not so much by general publicity aimed at the future as by improving or extending the existing arrangements by which large neighbouring hospitals supply the corneal grafting centres. Lord STONHAM: Is the noble Lord aware that at Moorfields, the largest centre for corneal grafting in the country, there is a waiting-list of never less than 100 cases, and that these people have to wait as long as eighteen months in unnecessary blindness?—Lord ST. OSWALD: I was aware of the figures at Moorfields. The areas where supplies are not considered adequate are North London, Sheffield, Manchester, and Liverpool. The position in those places has been kept under review and supplying hospitals reminded of the need.

The Earl of ARRAN: May I, as a governor of Moorfields Hospital, confirm the situation. Furthermore, may I ask whether the noble Lord is aware that this lack in donor material is entirely due to the restrictive operation of the Corneal Grafting Act 1952? Would he perhaps ask the Minister whether, in view of the sympathetic attitude of the public towards corneal grafting in general, he would consider giving unfettered effect to that Act? Lord ST. OSWALD: I think that what the noble Earl may be referring to is the power which is given to hospitals to rely simply on the absence of any known objection, but they have been advised by the Minister that wherever relatives are available their consent should be obtained. I think it is generally felt that were the former method adopted it would cause great public perturbation and would not be popular, but would be considered as being arbitrary. The Earl of ARRAN: The present situation is even more embarrassing. What happens now is that a patient dies and that, before his eyes can be used for this excellent purpose, his relations have to be asked—in other words, in the same breath they have to be told that their father, brother, or husband has died—can his eyes be used? Lord STONHAM: Would the noble Lord not suggest to the Minister that when people come into hospital and are asked to sign an agreement for postmortem, the words should be added to the form that they are willing, in the event of their decease and providing their relatives have expressed no objection, for their eyes to be used for therapeutic purposes?—Lord ST. OSWALD: My Lords, I am entirely in sympathy with the noble Lord's aims in regard to this matter, as everybody must be. I will certainly put forward his proposal to the Minister.

Superintendents of Mental Hospitals

Mr. WALKER-SMITH, the Minister of Health, has decided to make regulations revoking the National Health Service (Superintendents of Mental Hospitals, &c.) Regulations, 1948, as from the date of the coming into force of the main provisions of the Mental Health Act, 1959. The effect will be to put psychiatric hospitals in the same position as other hospitals in that there will be complete discretion whether or not a superintendent should be appointed. The new regulations will preserve the contractual rights of superintendents actually in post.

Obituary

SYDNEY WENTWORTH PATTERSON

M.D. Melb., D.Sc. Lond., F.R.C.P.

Dr. S. W. Patterson, lately senior physician at Ruthin Castle, died on May 1 at the age of 78.

He was born in Melbourne and he was always proud to consider himself a "good Australian". He qualified in 1905, and hard work, partly in remote country practice, enabled him in 1912 to come to University College, London, and work under Prof. E. H. Starling (whose daughter he later married). With Starling, he published work which is still regarded as important on cardiac output, heart-rate, and diabetes. The outbreak of war interrupted his physiological research and he served in France with the Australian Voluntary Hospital. Later he became assistant adviser in pathology to the B.E.F.

In 1919 he went back to Melbourne as director of the Walter and Eliza Hall Research Institute, but in 1923 he returned to this country to join the staff of Ruthin Castle Clinic in North Wales as the colleague of Edmund Spriggs. An old friend, Dr. J. H. Anderson, shortly followed him from Adelaide. Together the three men formed a successful team: they all cared for patients, and Patterson made a special contribution to the scientific and technical side of the work. He became senior physician in 1944 and retired only two years ago.

Patterson often spoke at meetings of the Association of Physicians, the Gastroenterological Club, of which he was president in 1953, the Medical Society of London, and the Heberden Society. He was Bradshaw lecturer at the Royal College of Physicians in 1941. He also published many papers and contributed articles to medical textbooks on widely differing subjects, but latterly most of his writings were on the alimentary system.

E. A. S. writes:

"With a patient Patterson was kind, thorough, perceptive, and astute. He talked discursively and had a curious mannerism by which the construction of a sentence would be changed in midflight, but his written reports were able summaries, and he vigorously pruned redundancies in his juniors' writings. He had a scholar's mind. It was, or seemed to be, a delight to him to discuss critically a physiological review with a student forty years his junior; or to search the British Museum and the Welsh National Library for old plans of Ruthin Castle and share with others his learning about local history. Such things, after his family, were his real interests, and when a very late retirement came, he chose to spend his old age in the laboratories of University College, London, in active experimental research on wound-healing with Prof. J. Z. Young.

"Patterson's industry was phenomenal, embracing his clinical and scientific work and in later years a good many administrative and financial responsibilities. All who knew him admired the energy he threw into the affairs of Ruthin Castle when some seven years ago its future, because of the impact of the health service, was temporarily uncertain. Real relaxation—except when he was with children—he seemed to find difficult. And his vigour off duty in the vegetable garden or the apiary or at the clock-repairing bench was hardly less remarkable than that at work."

Dr. Patterson is survived by his widow, their four daughters, and a son who is a plastic surgeon at Oxford.

CECIL HUGH MYDDLETON HUGHES

O.B.E., M.B. Lond., F.F.A. R.C.S.

Dr. Cecil Hughes, consulting anæsthetist to King's College Hospital, London, died at his home in Hove, Sussex, on May 2.

He was educated at Westminster School and at the Westminster Hospital. In 1900 he joined the South African Field Force and was posted to the Imperial Yeomanry field hospital. He had the surprising experience of being captured by the famous Boer general, de Wet, in person and of making his escape. After qualifying in 1903 Hughes held house-posts at Westminster before he was appointed administrator of anæsthetics, a post which he held until in 1914 he was appointed assistant anæsthetist to King's College Hospital. He was also anæsthetist to the Seamen's Hospital, Greenwich, the Samaritan Free Hospital, the National Dental Hospital, and the Bethlem Royal Hospital. In the 1914-18 war he was appointed consultant anæsthetist to the Royal Navy, with the temporary rank of surgeon-commander, and he served at the Royal Naval Hospital, Chatham, where he gave anæsthetics for Sir Watson Cheyne. He was appointed O.B.E. at the close of the war. In 1921 he became senior anæsthetist and lecturer at King's, and when he retired from the staff in 1936 he was appointed consulting anæsthetist. In the late war he returned to the King's sector and undertook anæsthetic duties at the Leatherhead Emergency Hospital.

He was both president and secretary of the section of anæsthetics of the Royal Society of Medicine, and during his term as secretary he was responsible for the arrangements for the centenary of the death of Henry Hill Hickman, and it was largely due to his endeavours that the Hickman medal for outstanding service to anæsthesia was instituted.

F. F. C. writes:

"As an anæsthetist, Hughes was an artist rather than a scientist. He refused to administer deep ether anæsthesia and confined himself to chloroform-ether mixture and spinal analgesia. He was a master of the art of light anæsthesia and enjoyed teaching this almost forgotten technique to his students, using a drop bottle and a Schimmelbusch mask covered with a single layer of lint. He insisted on attention to detail and woebetide the student who could not describe to him the signs of anæsthesia.

"Hughes was gentle and polite to everyone, patients, students, and staff alike. He was an ideal host who gave the impression that the comfort of his guests was his sole concern, and he was careful to make light and pleasant conversation to put entirely at his ease the junior whom he was entertaining. His fatherly, kindly manner earned for him the nickname of 'Daddy'."

IRENE YATES

M.D. Lond., M.R.C.P., D.P.M.

Dr. Yates, formerly psychiatrist to the Queen Elizabeth Hospital for Children, Hackney, and the Elizabeth Garrett Anderson Hospital, died in London on April 23 after many years of increasing physical disability.

She was born in 1894, the youngest of eight children of a Protestant family in Southern Ireland. She was educated at Alexandra College in Dublin and at the London School of Medicine for Women. After qualifying in 1918 she held house-appointments in London at her teaching hospital, the Brompton Hospital, and the National Heart Hospital. She was appointed assistant physician to the Elizabeth Garrett Anderson Hospital, but within a few years a long illness compelled her to resign. After her recovery she decided to take up psychological medicine and she worked at the Maudsley Hospital, taking the D.P.M. in 1932, and at private mental homes at Lincoln and Bristol. In the mid '30s she was reappointed to the staff of the Elizabeth Garrett Anderson Hospital, this time as psychiatrist. She was also appointed psychiatrist to the Queen's Hospital for Children but her work was again interrupted by illness, and after the outbreak of war she decided that she would do more useful work among schoolchildren in Somerset than in partially evacuated London. While in Somerset she began to have neurological symptoms, and though she struggled on till after the end of the war, her life from that time onwards was one of increasing physical disability.

H. M. M. M. writes: "As a student Irene Yates was popular; she was gifted socially and intellectually, with a quick Irish

wit, and she was a hard worker—but before she graduated she had a period of diplopia, presumably the first symptom of the disseminated sclerosis from which she died over forty years later. She maintained to the end her power to jest at her own troubles, her human interest in relatives and friends and those about her, as well as in the happenings in the world outside the four walls of her sickroom. A verse she sent to a friend one Christmas may well stand as epitaph to a gallant doctor and patient:

Sow as you will, reap as you sow . . .
Labour is hard, rich harvests slow.
Storms may flood, and drought may burn;
Good crops soon to ruin turn;
But seed and waiting ground remain,
Courage and will to start again.
Whether this year bring good or ill,
May we never lose hope and keep
Happiness still.

Diary of the Week

MAY 15 TO 21

Monday, 16th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Prof. C. H. Stuart-Harris: Virus Infections of the Respiratory Tract.

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2
5 P.M. Prof. R. R. Porter: Structure of Gammaglobulin and Antibodies. (Almroth Wright lecture.)

Tuesday, 17th

ST. MARY'S HOSPITAL MEDICAL SCHOOL
5 P.M. Dr. R. R. Willcox: Vaginitis Caused by Trichomonas and Candida Infestation.

SOUTH-WEST LONDON MEDICAL SOCIETY
8.30 P.M. (Bolingbroke Hospital, S.W.11.) Sir Eric Riches: Carcinoma of the Bladder. (Bolingbroke lecture.)

Wednesday, 18th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8.15 P.M. *General Practice.* Bishop of Durham: The Relation Between Parish Priest and Family Doctor.

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Prof. Robert Knox: Strategy and Tactics of Chemotherapy.

ROYAL FREE HOSPITAL, Gray's Inn Road, W.C.1
5.15 P.M. Dr. Alfred Gellhorn (New York): Medical Aspects of Cancer.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. J. O. Oliver: The Hæmopoietic System in Skin Diseases.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. N. S. Plummer: Bronchopulmonary Mycetomas.

UNIVERSITY OF BIRMINGHAM MEDICAL SCHOOL, Birmingham, 15
5 P.M. Sir Dugald Baird: Evolution of Modern Obstetrics. (First of two Ingleby lectures.)

Thursday, 19th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Professor Stuart-Harris: Virus Infections of the Respiratory Tract.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Dr. G. S. Nelson: Schistosomes as Zoonoses in Africa.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY
8.15 P.M. (11, Chandos Street, W.1.) Dr. J. A. Gorsky: An Historical Inquest and Exhumation.

UNIVERSITY OF BIRMINGHAM MEDICAL SCHOOL
5 P.M. Sir Dugald Baird: Evolution of Modern Obstetrics. (Second of two Ingleby lectures.)

HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. H. W. C. Griffiths: Crush Injuries of the Chest.

UNIVERSITY OF ST. ANDREWS
5 P.M. (Queen's College, Dundee.) Prof. Thomas McKeown: Human Prenatal Growth.

Friday, 20th

ROYAL SOCIETY OF MEDICINE
5.30 P.M. *Epidemiology and Preventive Medicine and Comparative Medicine.* Dr. C. H. Andrewes, Mr. H. V. Thompson, Miss Miriam Rothschild: Myxomatosis in Britain.

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M. Mr. Ian Orr: Selection of Operation for Peptic Ulcer.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.1
5.30 P.M. Prof. F. C. Ormerod: New Concepts of the Function of the Cochlear and Vestibule.

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
4.30 P.M. Dr. Denis Williams: Syndromes of the Basilar Artery.

Saturday, 21st

SOCIETY FOR THE STUDY OF INFECTIOUS DISEASES
11 A.M. (Ruchill Hospital, Glasgow.) Opening of one-day meeting.

Notes and News

EMPIRE RHEUMATISM COUNCIL

IN 1959 the Empire Rheumatism Council spent £56,000 on research, compared with £4600 in 1951. This progress is welcome, states Dr. W. S. C. Copeman, the chairman, in the report for 1959,[1] since every year 730,000 employed persons in Britain claim sickness benefit by reason of rheumatism, 27 million working days are lost, and the cost of the resulting absenteeism is estimated at £80 million. The Council is certain that the causes of rheumatism can be established if research is continued and developed.

Projects sponsored by this Council include the establishment of an electron-microscopy unit at St. Thomas's Hospital Medical School, London, under Dr. D. V. Davies, the professor of anatomy; the formation of an industrial rheumatism unit under Dr. J. J. R. Duthie, of Edinburgh, to study the social and economic effects of the disease in industry; and the setting up of a mobile field survey unit, the only one of its kind in the world, under Dr. J. S. Lawrence. Surveys by this unit have shown that one person in twenty in Britain has at one time or another suffered from an acute form of rheumatism (polyarthritis). This occurs most commonly towards the end of winter; although often severe enough to confine the patient to bed, it often disappears without permanent arthritis or heart-disease, and it is therefore important to distinguish this from the more serious forms.

Degeneration of intervertebral discs, a common complaint among manual workers, is sometimes connected with rheumatoid disease. These cases must be diagnosed so that correct treatment is given.

Work to determine the mode of action of aspirin is being carried on by Mr. R. J. Ladd at University College, London, who is studying its effect on blood-flow; by Dr. J. A. Hicklin at London Hospital Medical College, working on potassium exchange; and by Dr. V. Moses, who has shown that it inhibits enzyme synthesis with a consequent effect on both carbohydrate and protein metabolism.

Expanding activities are also reported from the Commonwealth. In Canada they are carried on through the Canadian Arthritis and Rheumatism Society, in Australia through the Australian Rheumatism Council (both Canada and Australia have separate professional associations, similar to the Heberden Society in the United Kingdom), and in New Zealand through the New Zealand Rheumatism Association (a combined medical and lay body). It is hoped to form a Council in South Africa in the near future.

AN EXPANDING INDUSTRY IN RADIOISOTOPES

THE talents of the versatile radioisotope are more and more in demand all over the world—in medicine, in biological and many other kinds of research, in industry. To meet some of this demand it is the special function of the Radiochemical Centre, a part of the United Kingdom Atomic Energy Authority, to produce and distribute the many radioisotopes and related products made available by the Authority for civil purposes. This commercial service radiates from Amersham, in the Chiltern Hills, 25 miles from London, and is available to all countries of the world. Until March of last year the arrangements for producing and marketing radioisotopes were shared between the Radiochemical Centre and the isotope division of the Atomic Energy Research Establishment at Harwell. At that time the scope of the Radiochemical Centre was extended to form a single comprehensive organisation with headquarters and principal laboratories at Amersham. During the first year under this new arrangement, the Centre handled some 35,000 consignments of radioisotopes, to a total value of over £1 million. 60% of the products went abroad.

Another stage in the expansion of the Radiochemical Centre was marked last week when two new laboratories were inaugurated by Sir Cyril Hinshelwood, P.R.S.

1. Issued by the Council, Faraday House, 8, Charing Cross Road, London, W.C.2.

The *organic laboratory* is designed for chemical and biological work with carbon 14 (^{14}C) and tritium, both isotopes of low toxicity which do not emit γ rays. No heavy screening is needed therefore, and the laboratory's equipment does not differ greatly from that of the modern organic chemistry laboratory. The organic department provides a liberal supply of labelled compounds for tracer methods used in science, medicine, and industry. At present about 230 ^{14}C-labelled compounds are listed in the Centre's catalogue. New compounds lately added include cortisone, cholesterol, decamethonium bromide, and nicotinic acid. About 50 tritium-labelled compounds are now available, including aminoacids, sex hormones, cortisone, folic acid, pyridoxine, and histamine. Of special interest is thymidine which is used to label nucleic acids in blood cells and to mark individual chromosomes. The organic laboratory also makes human serum-albumin labelled with ^{131}I for blood-volume measurements and metabolic studies, and ^{58}Co-labelled vitamin B_{12}.

The *alpha laboratory* works with radium and other naturally occurring radioelements, all of which are highly toxic and many are energetic γ-emitters. Heavy screening and remote-handling equipment are therefore needed. The " hot benches " are screened with 3–4 feet of concrete and up to 10 in. of lead. Within each 50-feet-long bench is a series of connected reaction boxes, served by an electric railway which carries active materials from one box to another. The work is performed by mechanical manipulators and watched through lead-glass windows up to 18 in. thick. This department produces, among other things, many therapeutic radium appliances; and there is a steady industrial demand for neutron sources, based on radium or polonium.

Production of basic isotopes, such as ^{131}I, ^{32}P, ^{35}S, and ^{198}Au, has been increasing at about 10–15% per annum; and the demand for several others (e.g., ^{51}Cr, ^{42}K, ^{24}Na, ^{132}I, ^{55}Fe, ^{59}Fe, and ^{45}Ca) has grown sufficiently to justify their routine production. ^{60}Co is now being produced on a very large scale in response to industry's demand for powerful γ-ray sources for processing various materials. Amersham supplied about 300,000 curies of ^{60}Co last year, the larger part of which went to a carpet manufacturer in Australia to provide the first commercially operated facility for sterilising bales of goats' hair against anthrax.

The Centre sends its cargoes to some 60 countries and half of all deliveries go by air. Sometimes a hermetically sealed can in a postal packet is enough to carry the goods; at other times the container must weigh several tons. The shortest-lived isotopes require very special plans for delivery, but even those with a half-life as short as a week can be sent to any part of the world by air. And the Centre, which is the only organisation in the world distributing natural *and* artificial radioisotopes on a commercial scale, gallantly charges its customers for only the radioactivity that reaches them, not for what was there when the isotope left Amersham.

ADMINISTRATION IN THE N.H.S.

AT a farewell presentation the speeches are usually congratulatory rather than stimulating. But to the colleagues who met in Glasgow on March 8 to recognise his retirement Dr. A. K. Bowman offered warnings rather than platitudes.[1] He has been senior administrative medical officer of the Western Regional Board since its start, and his remarks were based on eleven years' administrative experience in the National Health Service. He confessed that this had left him uneasy about the effect of the growing domination of lay administration on the future of medicine in this country. The people in charge of a human and personal service should be medically qualified and of high calibre, and their judgment and decisions should take precedence over the judgment and decisions of lay administrators. However competent a layman may be, and however anxious to secure the best results, he is, Dr. Bowman holds, neither by outlook nor training qualified to take command.

Unfortunately the power of the lay administrator was fostered by the statutory division of the medical members of the service into three groups. " So long as there remains that unpalatable division within the ranks of the profession, as dictated by law," Dr. Bowman said, " I see no means whatever of the profession being able to speak with the kind of resolution which is essential if their future status in this country is to be maintained." He saw the revision of this artificial division as a matter of urgency. But there were also deficiencies inside the profession and these could be made good only from within. The profession must set its own house in order if they were to achieve the status and influence necessary to win " professional freedom within the setting of common liberty ".

1. *Glasgow Herald*, March 8, 1960, p. 5.

EXPIRED-AIR RESUSCITATION

TWO recent films on artificial respiration by the expired-air method have lately become available in this country. *That They May Live* (16 mm. sound, colour, 28 min., Canada, 1959) was made by Dr. A. B. Dobkin and Dr. M. H. Brook at the University of Saskatchewan College of Medicine. It is the story of a reporter who learns about resuscitation by the mouth-to-mouth method and has the opportunity to apply it himself on the same evening. Recalling that the method used on President Lincoln to save his life in 1865 was adopted by the United States Army and American Red Cross only in 1957, an anæsthetist demonstrates the improved respiratory exchange in an anæsthetised curarised subject by expired-air respiration as compared with the conventional methods of artificial respiration. The procedure using Dr. Brook's airway is then shown, and several situations where mouth-to-mouth respiration may be lifesaving are enacted. This interesting film makes a good case for the routine adoption of this procedure by all first-aiders and others likely to meet the emergency. Special emphasis is laid on the hygiene of the method—notably, placing a napkin between the patient and the rescuer or using a Brook airway. Though the story is rather contrived, the film is very suitable for showing to all members of rescue organisations and includes nothing to offend the squeamish.

Respiration Resuscitation Techniques (16 mm. sound, colour, 40 min., U.S.A., 1958), made by Dr. Peter Safar, is a laboratory investigation of the efficiency of several methods of artificial respiration in the hands of trained and untrained rescuers. After a brief description of the apparatus used, volunteers are anæsthetised and given a short-acting relaxant. Artificial respiration is then performed by positive pressure from an apparatus, and by the Sylvester, Holger-Nielsen, and mouth-to-mouth methods while the volume of gases exchanged or the chest expansion and the percentage oxygen and carbon dioxide in the blood are recorded. The experiments are repeated by trained and untrained first-aiders, and it is said that 167 untrained people took an average of 40 seconds to learn insertion of the airway for mouth-to-mouth respiration, and 60 seconds to instil over 500 ml. of air into the subject on the first attempt. In an apnœic subject after 30 seconds, oxygen saturation was less than 80% but after six breaths into the subject by the rescuer it returned to 95%. The film emphasises that the conventional artificial-respiration techniques may prove unreliable and sometimes impossible to apply, and that mouth-to-mouth respiration gives adequate oxygenation in seconds before any apparatus arrives on the scene. This film is designed for the scientist rather than the layman, so the demonstration of " wrong methods " is justified. The argument is convincing and the inclusion of the appropriate oximeter readings and the spirometric and pneumographic tracings in the picture with the technique being shown is commendable. This is a film for those responsible for training members of rescue organisations.

That They May Live may be obtained on free loan from Smith and Nephew Ltd., Bessemer Road, Welwyn Garden City, Herts; and *Respiration Resuscitation Techniques* is available from the Medical Director-General of the Navy, Queen Anne's Mansions St. James' Park, London, W.1.

In a note in our issue of April 30 we wrongly stated that the Brook airway and other training aids were supplied in this country by W. H. Bailey & Sons, Ltd. In fact Smith and Nephew, Ltd., Bessemer Road, Welwyn Garden City, Herts., have the exclusive selling rights of the Brook airway and training aids (manikin and cutout) for the United Kingdom and the world with the exception of the United States and Canada. All inquiries should be addressed to them.

REGIONAL HOSPITAL BOARDS AND BOARDS OF GOVERNORS

THE following doctors have been newly appointed to boards. They will hold office till March 31, 1963.

REGIONAL HOSPITAL BOARDS

Sheffield.—R. J. Donaldson, A. W. Kay.
North West Metropolitan.—J. D. S. Flew.
South Western.—R. V. Cooke.
Manchester.—T. S. Heslop.

BOARDS OF GOVERNORS

London Hospital.—C. F. Barwell, E. C. B. Butler, and Louis Comyns (till March 31, 1962).
Royal Free Hospital.—Frances Gardner, P. E. Thompson Hancock.
Middlesex Hospital.—F. C. Golding, W. R. Winterton, and A. J. B. Goldsmith (till March 31, 1962).
Charing Cross Hospital.—A. R. Makey.
St. George's Hospital.—J. H. Hovell, Wylie McKissock.
Westminster Hospital.—J. L. Franklin.
St. Mary's Hospital.—G. B. Mitchell-Heggs and I. G. Robin (till March 31, 1962).
Guy's Hospital.—R. J. Cann.
King's College Hospital.—J. S. S. Fairley.
St. Thomas's Hospital.—H. J. Wallace.
Hammersmith, West London and St. Mark's Hospitals.—Clifford Morson.
Royal National Throat, Nose and Ear Hospital.—I. Friedmann.
Moorfields Eye Hospital.—C. A. Cook.
Bethlem Royal and Maudsley Hospitals.—B. G. C. Ackner, J. R. Ellis.
St. John's Hospital for Diseases of the Skin.—J. E. M. Wigley.
Hospitals for Diseases of the Chest.—J. R. Belcher.
Royal National Orthopædic Hospital.—C. W. Manning, P. G. Walker.
National Heart Hospital.—J. M. H. Campbell.
Royal Marsden Hospital.—A. H. Hunt.
Eastman Dental Hospital.—Robert Bradlaw, R. R. Stephens.
United Leeds Hospitals.—George Armitage.
United Sheffield Hospitals.—I. B. Sneddon.
United Cambridge Hospitals.—D. G. Bratherton, A. J. Rook.
United Oxford Hospitals.—J. L. Boldero, H. R. Vickers.
United Bristol Hospitals.—C. A. Brown, R. E. Horton.
United Birmingham Hospitals.—W. T. Cooke, A. B. MacGregor.
United Manchester Hospitals.—A. Morgan-Jones.
United Liverpool Hospitals.—A. R. D. Adams.

HANDBOOK ON PRESCRIBING

A COMPREHENSIVE handbook on prescribing is being sent by the Ministry of Health to all doctors engaged in the National Health Service and to final-year medical students. The handbook, prepared in consultation with the British Medical Association, includes the following sections: (1) general information about prescribing under the National Health Service; (2) the cost of *National Formulary* preparations and of some proprietary preparations, with the cost of any equivalent or similar standard preparations; (3) extracts from the Drug Tariff; (4) report on the definition of drugs by the Standing Joint Committee on the Classification of Proprietary Preparations (Cohen Committee); (5) list of proprietary medicines advertised direct to the public; (6) list of proprietary preparations classified by the Cohen Committee as consisting of, or containing, drugs which the committee does not regard as of proved therapeutic value; and (7) extracts from past editions of *Prescribers Notes*. The preparation of such a handbook was recommended by the Hinchliffe Committee.[1]

University of Oxford

On April 28 the following degrees were conferred:

D.M.—* F. I. Caird, Anthony Ryle.
M.Ch.—* R. T. Campbell.
B.M.—D. G. Sargant.

* In absentia.

University of Cambridge

On April 30 the following degrees were conferred:

M.D.—J. E. Forster, D. R. Bowsher, C. D. Evans.
M.Chir.—* W. G. Williams.
M.B., B.Chir.—* D. A. Wright.
M.B.—Alexander Harley, P. J. N. Howorth, R. A. Lewin, * M. J. Orrell, Peter Snell, D. F. L. Watkin.

* By proxy.

1. Interim Report of the Committee on Cost of Prescribing. H.M. Stationery Office, 1958. See *Lancet*, 1958, ii, 1376.

University of London

Dr. Michael Shepherd, senior lecturer in psychiatry at the Institute of Psychiatry, has been appointed to the readership in psychiatry at that institute.

The degree of M.D. has been awarded to the following:

P. T. Flute, D. F. N. Harrison, R. J. Shephard.

On March 8 the degree of PH.D. in the faculty of medicine was awarded to E. J. K. Penikett.

University of Wales

On July 22 the honorary degree of D.SC. will be conferred on Dame Janet Vaughan.

University of Exeter

On May 4 the honorary degree of LL.D. was conferred on Dr. C. J. Fuller.

Royal College of Obstetricians and Gynæcologists

The following have been awarded the D.OBST.:

Margaret E. Abel, Shirley A. P. Abell, Eleanor M. Adams, J. F. R. Adams, Alexander Addison, Delia M. Aitken, Razia Akbani, John Armstrong, J. R. Ashwood, Derek Atkinson, F. G. Atkinson, Safiya Azimuddin, J. K. Baird, Robert Baird, Ramala Bakaya, P. J. Ball, R. M. Barnes, Maureen E. Barr, D. G. Barrowcliffe, Ivy Barua, J. F. S. Batson, J. T. Bavington, J. R. Bell, M. S. Benett, R. B. Bennet, M. J. P. Berkley, L. S. Bernstein, F. A. Best, G. J. Biggam, Margaret A. Birchall, T. A. P. Birkett, H. E. Black, Paula D. Black, Margaret I. Blackhall, H. R. Blair, A. J. Blakeman, J. R. Blatch, A. I. Blenkinsop, Reuben Bolton, G. T. K. Boughey, C. J. Briglmen, J. M. Bristow, James Brosnan, A. H. Brittain, H. C. I. Bywater, J. R. Burwell, G. L. Caley, Ian Capperauld, C. J. Carr, J. V. F. Catto, A. J. McM. Cavenagh, E. C. Cawte, Theam Kheng Cheah, J. P. Ah Fee, Chui Wan Cheong, J. M. Clark, C. B. Clennar, Marjory Clowsley, J. H. Cochrane, M. D. Coulter, Izette R. Coulton, G. F. Counsell, George Cowie, John Coyer, T. A. Crantock, A. D. Crawford, Alison S. E. Crewdson, Katharine E. Cuthbert, P. G. Dale, Shyamoli Datta Chowdhury, Denzil Davies, Gwyneth M. Davies, H. T. Davies, L. M. Davis, J. A. Davis, Brigid C. C. Davison, Hugh Dawson, Lalita V. Deshpande, Charles Diamond, W. R. Dick, B. C. Dixon-Warren, Phyllis E. D'Netto, K. E. Doran, G. S. Duncan, H. J. H. Dunn, Douglas Eakins, Vasos A. Economides, Elizabeth M. Edmunds, J. G. Elias, Elizabeth Elliott, P. J. Ellis, R. W. Elsdon-Dew, L. A. Emanuel, P. J. Enoch, C. D. G. Evans-Prosser, M. W. Everitt, D. R. Farmer, B. E. Farnham, L. J. Farrow, Biyagamage Aaron Fernando, Nurjahan Ferozuddin, H. W. Fladee, I. M. Fletcher, Janet A. Fletcher, Kevin Flintan, H. B. B. Forshaw, William Fox-Russell, H. J. L. Francis, P. I. Frank, A. K. Fulton, N. H. N. Gardner, P. T. Gardner, Ramon Gardner, A. J. A. Garlant, T. H. Geddis, Jennifer M. R. Gilchrist, A. A. Gildersleve, P. G. Gillam, P. J. Gillies, R. T. Glen, J. E. Godrich, H. L. Goldwater, D. J. Goodman, I. S. Governor, C. B. T. Grant, Ellen C. G. Grant, J. N. S. Green, R. C. Grieve, Monica M. Gurnhill, Savitri Gurung, D. D. Guy, C. A. A. Haigh, K. C. Hammond, Margaret E. Hanlon, D. R. W. Hartley, D. C. Harvey, Beryl Heap, W. R. Heaton, Ronald Heslop, Anne S. Hill, D. M. C. Hislop, E. J. Horgan, J. L. Horner, G. R. Horton, Janet M. Houlston, Judith C. Howard, Mary S. Howell, Khin Khin Htway, H. I. Humphreys, G. B. Hunt, Florence Suhasini Iswariah, Irene M. J. Jackson, Trefor Jenkins, H. C. Jennings, H. H. John, Saramma John, A. D. S. Johnson, R. W. Jones, V. D. Jones, Mary O. Joseph, Haddad Omer Karoum, Audrey King, H. J. Kosasky, Sylwester Krzaniak, I. McA. Kyles, H. O. Latham, A. B. Lavelle, A. R. Leader, Eva H. Letchner, Leslie Lewis, Thomas Lind, Rhona Lindup, H. K. Litherland, Nesta E. Lloyd, J. A. London, Conn Lucey, Grania McCarthy, S. F. McCarthy, D. R. McCoy, J. S. McCracken, K. H. McCraith, A. H. MacDonald, B. M. McGibbon, R. D. Macgill, D. B. MacGregor, Daniel McLeman, June M. McLeod, I. S. Macmillan, A. D. McNeill, J. M. Maguire, Frances Shao Fen Mao, John Martin, John Mason, B. S. Mather, Gul Mathew, Ma Tin May, M. A. Melsom, P. H. Merry, J. C. Merrington, John Miller, Margaret Miller, Patricia A. R. Miller, A. R. Milne, C. A. Milner, B. A. E. Mindham, Zakia Minhas, A. V. Mitchell, Katherine M. Moore, D. J. Moorehouse, H. M. Moorhouse, D. H. Morgan, A. B. Morphy, J. L. Morrison, Bhati Mukherjee, J. P. Mumford, D. F. Munro, Murdoch Murchison, Koshu Vishindas Narumalani, Marjorie S. Newton, W. P. L. O'Driscoll, S. S. I. Parker, H. V. Parry, Mary W. Parry, A. G. P. Paton, P. W. S. Patton, G. W. Peacock, J. L. Penny, J. H. Perry, Mary Philipose, R. M. Phillips, Raymond Pilkington, A. J. Pim, Sylvia J. Pinder, H. D. W. Plowright, Mary S. Plumbly, Donald Powell, C. J. Primmer, D. J. H. Prosser, R. L. Pyle, J. D. Raiman, Chitra Rao, M. J. Raphael, L. R. Redman, Marguerita Regan, Elizabeth M. Riddell, C. J. Roberts, K. K. T. Robertson, K. D. Robinson, F. D. Roche Kelly, L. C. Rose, D. F. Rowlands, Satyavathi Roy, Indu Bhusan Roy Chowdhury, D. G. L. K. Russell, I. A. Ruthven-Stuart, M. E. R. Samson, Algine Miliana Sansoni, Harendra Nath Sarmah, J. M. Scott, R. S. C. Scoular, A. M. Segal, C. A. Selway, R. A. Sharpe, M. C. Sharrard, M. G. Shelton, K. I. Shimmings, Joyce K. Siromoni, B. A. M. Smith, R. N. Smith, Stanley Sorkin, F. M. Spence, P. D. Sprackling, J. A. Stainton-Ellis, J. T. Stewart, Kyu Kyu Swe, Ernest Taylor, J. G. Thomas, Anne E. Treharne, M. E. Tuck, J. L. Tuton, J. C. Twomey, V. R. Twyman, I. H. M. Veitch, Julian Viner, Umathevan Viswalingam, R. O. Walker, Sheila J. Wallace, M. T. Ward, A. F. Watson, Nancy M. Watts, J. L. Webster, John Weston, B. R. Wheeler, D. M. Whiteford, Nora E. Wild, R. E. Wild, M. C. T. Wilkes, R. K. Wrennall, A. F. Wright, Oon Hock Yeo, Carmen Ka Man Yuen.

Rockefeller Foundation

During the first quarter of 1960 the Foundation distributed $4,489,000. Grants for medical and natural sciences amounted to $1,497,000 and included a five-year grant of $50,000 for Sir Hans Krebs' research, at the University of Oxford, on cell metabolism, and a further grant of $25,000 during the next three years for Dr. T. R. R. Mann's research, at the University of Cambridge, on reproductive physiology.

Royal College of Physicians of Edinburgh

At a meeting of the college on May 3, with Dr. A. Rae Gilchrist, the president, in the chair, the following were elected to the membership:

E. McC. McGirr, R. N. Johnston, D. S. Smith, Battulapalli Ananta Ranga Rao, Robert Lamb, N. E. Loos, F. D. Honneyman, E. A. M. Wood, T. C. Nicol, Anantanarayana Ramasubramanian, J. K. Davidson, Bashir Hasan Khan, Narayan Shamsunder Dixit, Jagadish Narayan Mishra, Majid Ali Jafri, Sheila Pereira, J. S. Madden, I. W. Pinkerton, Isabella C. Ferguson, W. G. Wenley, Bryan Ashworth, Pamela M. Lambden, Ralph Shulman, Poi Kwong Wong, R. G. Sourjah, G. J. Addis, Kalvyn Schoeman Van Eeden, Benjamin Cooper, P. D. Moylan, Kantibhai Chaturbhai Patel, P. A. Barker, Sharda Ranjan, Surinder Kumar Vohra, John Johnson, Gopal Chand Pandey, J. H. P. Willis, Om Parkash Thaman, I. H. Jones, J. N. G. Davidson, B. S. L. Kidd, B. R. Knowles, Gopalakrishna Thagathuveettil Damodara Panicker Pillai, Braja Mohan Goswami, Peter McDonald, Alexander Pringle, Enid J. Cartwright, Aung-Than-Batu, Gilbert Obiafo Onuaguluchi, Aswathnarain Nagaraj, Sudarshan Kumar, Brajjeshwar Mittra, A. E. Charaoui.

Royal College of Surgeons of Edinburgh

At a meeting on May 6, with Prof. John Bruce, the president, in the chair, the following were admitted to the fellowship:

J. G. Allman, J. H. F. Batstone, Niren Bhaduri, W. H. Bisset, D. G. Calvert, Kenneth Chambler, R. G. Clark, Michael Cohen, B. C. Cohney, D. H. Coop, Delia M. H. H. Cothay, Chhaganlal Nanji Dedhia, E. E. Denman, H. C. De Wet, Mohamed Magid Ismail Fakhr, A. D. George, Mavis G. Gilmour, Peter Gortvai, Prithi Singh Grewal, J. M. S. Hague, M. A. Henderson, W. H. Huffam, K. F. Hume, E. G. Ibach, J. D. Iswariah, T. E. Jeffreys, C. O. R. King, W. J. Laister, G. J. Little, Peter Mactaggart, D. J. McWilliams, Hashim Makki, G. B. Markey, B. C. Meehan, Bharat Vrajlal Mehta, J. M. Mistry, Rajendra Nath Mullick, G. A. I. Namsoo, Cheuk Hing Ng, J. A. O'Reilly, W. McN. Orr, P. Mathai Paulose, Vithal Gangadhar Phansalkar, W. J. Poate, L. W. Poole, Abdul Aziz Qazi, R. A. Rivett, J. S. Scougall, D. K. Sutton, Chee Yong Tan, D. S. Thomson, Jayaweera Bandara Wedande, S. B. Williams, Kean Hong Yeoh.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting on May 2, with Mr. Arthur Jacobs, the president, in the chair, the following were admitted to the fellowship, *qua* surgeon:

A. K. Bain, D. Pui-Chee Chan, W. G. Millar.

Postgraduate Medical School of London

South Africa has raised £50,000 towards the building appeal of the school. The money has been given by business concerns and private individuals in response to an appeal launched in Johannesburg a year ago.

Nuffield Foundation

The Foundation has allocated £60,000 to form a " unit for the history of scientific ideas " which will produce educational films and books under the direction of Dr. Stephen Toulmin, formerly professor of philosophy at the University of Leeds. The first aim of the unit will be to produce a basic collection of teaching films and textbooks for use in sixth forms and introductory university courses in the history and philosophy of science.

Beit Fellowships

The following elections to fellowships have been made:

Junior fellowships (£900 a year).—D. C. Watts, M.SC. Lond. (at the department of biochemistry, University College, London); J. R. Casley-Smith, M.B., B.SC. Adelaide (at the Sir William Dunn School of Pathology, Oxford); P. F. Fottrell, M.SC. N.U.I. (at the tissue culture laboratory, biochemistry department, University of Glasgow); A. J. Rowe, M.A. Cantab. (at the Department of Colloid Science, Cambridge); C. F. V. Seaman, PH.D. Cantab. (at the Department of Medicine, Cambridge).

Senior fellowship (£1300 a year).—J. R. Tata, M.SC. Bombay, D.SC. Paris (at the National Institute for Medical Research, Mill Hill, London).

World Health Assembly

Opening the thirteenth World Health Assembly in Geneva on May 3, Sir John Charles, chief medical officer to the Ministry of Health, the outgoing president, said that today W.H.O. was concerned with two main groups of problems: first, environmental, nutritional, and epidemiological questions in the emergent States; and secondly the needs of the middle-aged and elderly in the other communities. It was a mistake to think that these were entirely separate sets of problems; they required the same approach for their solution—research, education, and cooperation.

Dr. H. B. Turbott, director-general of health, New Zealand, was elected president of the Assembly.

British Institute of Radiology

On Thursday, May 19, at 8 P.M., at the institute, 32, Welbeck Street, London, W.1, Dr. V. E. Cosslett will give the Silvanus Thompson lecture. He will speak on X-ray microscopy.

Mental After Care Association

The annual general meeting of this association will be held on Tuesday, May 17, at 3 P.M., at the Hall of the Worshipful Company of Haberdashers, Staining Lane, London, E.C.2. The speakers will be Monsieur L. C. Picalausa, director-general of the Belgian Red Cross, and Dr. Henry Yellowlees.

Société Médicale Internationale de Photo-cinématographie et Télévision Endoscopiques et de Radiocinématographie

This society will hold its annual congress on May 25 at 2.15 P.M., at 1, Wimpole Street, London, W.1. The speakers will include Dr. E. Chérigié, Dr. N. Jaupitre, Dr. M. Noix, Dr. Dubois de Montreynaud, Prof. P. Porcher (France), Prof. van d. Plaats (Holland), Prof. R. Janker (Germany), Prof. Chevalier Jackson (U.S.A.), Dr. J. J. Stevenson, and Mr. H. G. Hanley.

Zoological Society of London

The Ford Foundation has made this Society a grant of 550,000 dollars (about £196,000) to endow research fellowships in animal reproduction. The first awards will be made during the coming summer by a committee of experts and it is hoped that the Zoological Society fellows will have a secondary attachment to a university laboratory engaged in related work. Laboratories will be provided at Regent's Park by the society, and a Breeding Research Committee including Prof. E. C. Amoroso, Prof. F. W. Rogers-Brambell, Prof. A. St. G. Huggett, and Dr. A. S. Parkes will supervise the work.

Surgeon Rear-Admiral W. V. Beach has been appointed an honorary surgeon to the Queen in succession to Surgeon Vice-Admiral Sir Cyril May.

Dr. D. J. West, senior registrar to the forensic unit, Maudsley Hospital, London, has been appointed assistant director of research at the Institute of Criminology, Cambridge.

Brigadier H. L. Glyn Hughes will speak at the annual general meeting of the Elderly Invalids' Fund at Skinners Hall, 8½, Dowgate Hill, London, E.C.4, on Thursday, May 19, at 5.30 P.M.

The annual dinner of the Indian Medical Service Dinner Club will be held at the East India and Sports Club, St. James's Square, London, S.W.1, on Friday, June 10, at 7.30 p.m. Tickets may be had from the secretary of the club, Medical Room, Commonwealth Relations Office, Matthew Parker Street, S.W.1.

Appointments

DUCKSBURY, CHRISTINA F. J., M.B. Edin.: assistant M.O.H. and school M.O., Sheffield.

MERCER, J. C. G., M.B. Edin., D.C.H.: medical superintendent, East Fife hospitals board of management.

STEVENS, P. R., M.R.C.S., D.O.: consultant ophthalmologist, Blackburn and district group of hospitals.

TOWNSEND, MARY, M.B. Lond., M.R.C.P., D.C.H.: assistant M.O.H. and assistant school M.O., Dorset.

VALE, R. J., M.B. Lond., M.R.C.P., F.F.A. R.C.S., D.A.: consultant anæsthetist, Chelsea Hospital for Women, London.

WALLIS, ETHEL M., M.B. Edin., D.OBST., D.P.H.: senior assistant M.O.H., Oxford.

WHEBLE, V. H., B.M. Oxon, F.R.C.S.E.: consultant traumatic and orthopædic surgeon, Ashton, Hyde, and Glossop group of hospitals.

The Hospital for Sick Children, Great Ormond Street, London:

MISHRA, J. N., M.B. Patna, M.R.C.P.E., D.C.H.: medical registrar.

PISARELLO, J. C., M.D.: resident officer, departments of neurology and neurosurgery.

RANSOME-KUTI, OLIKOYE, M.B. Dubl.: assistant M.O., Tadworth Court.

Liverpool Regional Hospital Board:

BUXTON, P. H., M.D. Cantab., M.R.C.P.: consultant pathologist, regional neurosurgical unit, Walton Hospital.

CLARKE, E. E., M.D. N.U.I., M.R.C.P., D.P.M.: assistant psychiatrist, Rainhill Hospital.

COULSHED, NORMAN, M.D. Lpool, M.R.C.P.: consultant physician in cardiology, regional cardiac centre, Sefton General Hospital.

SCANLAN, E. P., M.B. N.U.I., D.OBST., D.P.M.: assistant psychiatrist, Rainhill Hospital.

SLATTER, K. H., M.D. Lpool, M.R.C.P.: consultant neurologist, regional neurosurgical unit, Walton Hospital.